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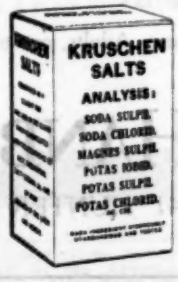

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UPPER RESPIRATORY TRACT INFECTION.[1]

By F. M. BURNET,

From the Walter and Eliza Hall Institute of Research in Pathology and Medicine, Royal Melbourne Hospital, Melbourne.

I AM concerned tonight with the commonest of all human diseases and the most difficult to prevent—colds, influenza and the like. In the army the diagnostic label is "U.R.T.I."—upper respiratory tract infection. Military hygiene at least in temperate climates has been able to reduce to negligible proportions the incidence of the classical war diseases, typhus, dysentery and enteric fever; but it has still failed conspicuously to deal with the respiratory tract infections. During the first world war American troops lost nearly as many days from duty on account of respiratory infections as from all other causes combined, while the number of primary admissions to hospital for influenza and bronchitis was well over 1,000,000 (Councell[(1)]). To come nearer home, in Victorian military camps during last winter approximately 16,000 cases of "U.R.T.I." were reported during the four winter months of May, June, July and August, of which 5,000 or 6,000 were probably due to the influenza epidemic in May and June. To give further figures would be merely to stress the obvious. During the last two winters we have been engaged on the study of influenza as it occurs in military camps and of the possibility of developing means of protective immunization against the more important types of influenza. In this lecture I shall deal mainly with specific virus influenza largely on the basis of our own work; but as virus influenza is by no means the only component of "U.R.T.I.", I have tried to keep a sense of perspective by discussing it as one member of a group of related conditions rather than as a wholly independent entity.

The Ætiology of the Common Respiratory Tract Infections.

According to average opinion, both lay and medical, there is a continuous range of simple respiratory infections, increasing in severity from the mild type of common cold through various degrees of feverish colds to influenza. Influenza itself may be mild or severe, the greatest intensity being shown in the still well-remembered pandemic of 1918-1919. There is a good deal to be said for the possibility that this popular opinion will eventually be shown to have a sound ætiological basis; but at the present time our accurate knowledge is confined to the infections lying in the middle of this range. Typical influenza epidemics are known to be due to infection with one of two related viruses—influenza viruses A and B. Methods of studying these viruses are now readily available, and a great deal is known about the viruses and about the experimental infections which they produce. Rather less is known about finer details of the human infection; but at least the disease can be defined and recognized on an ætiological basis—always the first step toward eventual control.

The causes of the common cold and of the various types of feverish cold and sporadic "influenza" at the one end of the scale, and of pandemic influenza at the other, remain unknown. There is a considerable volume of experimental evidence that typical colds are primarily due to a filterable virus or group of viruses. The work of Dochez[(2)] and his collaborators on chimpanzees and carefully quarantined human volunteers leaves little doubt that such is the case; but it is curious that during the last five or six years practically no work has been published on the subject, despite the great activity in all other fields of virus research. It is at least certain that if a "colds" virus exists, it has no power to infect the various laboratory animals which are susceptible to influenza viruses. Only the human being and his kinsman the chimpanzee can apparently be infected. Another curious finding is that of Kerr[(3)] and his collaborators, that when a group of volunteers lived constantly in a room kept at optimal temperature and humidity it proved impossible to transfer colds from one person to another.

My own impression, from fairly extensive reading, and from a considerable experience of fruitless attempts to isolate a virus from the nasal secretion of persons suffering from acute colds, is that progress must wait on the development of some new method of tackling the problem. Common experience indicates that there is some infective

[1] Read at a meeting of the Victorian Branch of the British Medical Association on August 4, 1943.

element involved, probably a virus or group of viruses; but some particular condition of the soil (the nasal mucosa) must also be present to allow effective planting of the infection. Seasonal changes obviously play an important part. Earlier work on the gross bacteriology of the throat has shown conclusively that during the winter months the potential pathogens streptococci, pneumococci and Pfeiffer's bacillus are more frequently present and tend to colonize a wider area of the respiratory tract than in summer. It is reasonable to suppose that the same conditions as make it easier for these bacteria to flourish increase susceptibility to low-grade viruses.

To turn to the other extreme of this range of respiratory infections, the influenza pandemic of 1918-1919 was a unique episode in the history of disease. It was, both in character and in extent, something very different from the former pandemics (those of 1847 and 1890-1893, for example) with which it is ordinarily linked. We do not know that it was due to an influenza virus and we probably never can know. The universal opinion amongst epidemiologists and virus research workers is, however, in favour of the view that the pandemic was one of influenza, essentially similar to the less-severe epidemics which have been studied in recent years. (For a discussion of the evidence for this view, the monograph by Burnet and Clark[1] may be consulted.)

The Experimental Study of Influenza.

On the sound rule of proceeding from the known to the unknown, it will be best to discuss the general pathology of the respiratory tract infections by taking influenza virus infections as a type. It is probable that both the milder and the more severe types of infection represent essentially variations on the same general theme.

Though it is perhaps not strictly necessary to the argument, it will be advisable, I think, to give an outline of the experimental methods now being used for the isolation and study of influenza viruses. The first method of isolating influenza virus was by inoculation of throat washings, filtered or unfiltered, into the nose of a ferret. In the ferret a febrile infection closely resembling human influenza was set up, and by suitable experimental methods the ferret infection could be identified as influenza. The ferret is still the only laboratory animal in which clinical influenza can be produced, and it is still indispensable for some types of work. Nowadays, however, both for isolation and for the production of immunizing material, the centre of the stage is occupied by the chick embryo.

Figure I is a rough diagram to show the arrangement within the egg of the various membranes and cavities of a ten to twelve day chick embryo. The chief points

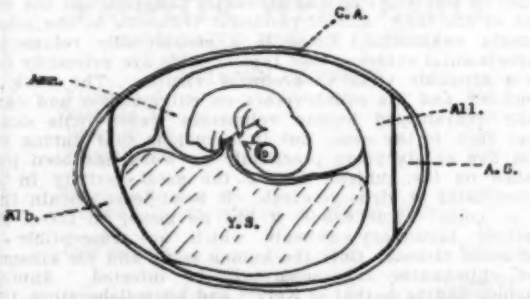

FIGURE I.

Diagram of chick embryo at about tenth day of incubation. Amn. = amniotic cavity; this is used for isolation of virus from human material. All. = allantoic cavity, used for production of the virus used in immunisation procedures. C.A. = chorio-allantoic membrane. A.S. = air space. Alb. = albumen sac. Y.S. = yolk sac.

to be recognized are, first, the chorio-allantoic membrane lying immediately under the shell membrane and acting as the embryo's lung. Beneath this is the large allantoic cavity, an outgrowth from the gut, which at the period we are considering contains about eight to ten cubic centimetres of clear allantoic fluid. The chief function of the cavity is to act as a receptacle for the chick's excreta. As development goes on, the fluid becomes turbid with urates. The embryo itself lies in the amniotic cavity, which is much smaller than the allantoic cavity and contains fluid rich in protein. This fluid communicates directly with the interior of both the digestive and the respiratory tracts of the embryo. Finally, there is the yolk sac, an outgrowth from the embryo, with a structure resembling that of intestinal mucosa. Highly vascular villi dip into the substance of the yolk and utilize it for the nutrition of the embryo.

In our laboratory the standard method of isolating influenza virus is to prepare a filtrate free from bacteria from garglings of a patient in the early stage of the disease. About 0·25 cubic centimetre of this filtrate is inoculated into the amniotic cavity of several eleven or twelve day embryos. The eggs are sealed and incubated at 35° C. for three, or more usually, for four days. They are then opened and the amniotic fluid is removed aseptically. If an infection has been produced, this fluid is present in increased amount, is lightly turbid and contains a high concentration of virus. In the original form of this technique, the existence of infection was recognized by making smears of the cells thrown off from the infected embryo lungs (Burnet[3]). A much more convenient method is to make use of a curious phenomenon described by Hirst[6] in 1941. If the infected amniotic fluid is diluted serially in saline solution, say from 1:10 to 1:640, and washed red cells (human or guinea-pig) are added, agglutination of the cells occurs in the higher concentrations, the reaction disappearing at dilutions in the range of 1:80 to 1:640. This agglutination apparently results from adhesion of the influenza virus particles to the surface of the red cell. A virus particle already attached to one erythrocyte can still attach itself to another and so act as a bridge between the two. Multiple bridges of this sort are responsible for the clumping of the cells.

The Hirst agglutination reaction can be applied in various ways for the characterization of the isolated strains. By the use of different types of red cell, it is possible to follow the process by which the virus becomes adapted to grow more readily in the chick embryo, losing its virulence for human beings in the process. When first isolated, it has little or no power to agglutinate fowl cells, although it is active against guinea-pig or human cells; with adaptation it eventually agglutinates fowl cells more readily than those of any other species. Another characteristic of the original "human" type of virus is that it will multiply only in the amniotic cavity or in the yolk sac. With adaptation, however, it readily develops the power to infect the cells lining the allantoic cavity, and whenever large amounts of virus are required for any purpose, such adapted strains are used.

Practically all types of influenza vaccine are now made by inoculating by a very simple procedure small amounts of an appropriate seed virus into the allantoic cavity. After two days' incubation, eight or ten cubic centimetres of lightly turbid fluid can be obtained from each egg. The fluid contains about 10^8 infective doses of virus per cubic centimetre, it is free from bacteria, it contains relatively little extraneous material and it has a physiologically balanced content of salts. One can hardly imagine more suitable starting material for the production of a virus vaccine, or for many other types of experimental work.

One other feature of experimental investigations on influenza requires a brief description. This is the measurement of antibody changes in persons infected by or immunized against influenza virus. In order to establish the fact that a true influenza virus infection has occurred, one may either isolate the virus or alternatively show that immediately after infection a rise in the amount of the corresponding antibody has occurred. There are several methods of doing this. The simplest is to make use of the Hirst agglutination reaction. Influenza antibody in adequate amount will prevent the agglutination of red cells by the virus, and it is easy to apply this fact to the

devising of a quantitative method of measuring the amount of antibody in a given sample of serum. The method is extremely simple to carry out, and within certain limitations it provides all the serological information normally required. There are several other methods of estimating the amount of neutralizing antibody, but they are all more time-consuming and expensive than Hirst's method.

The difference between influenza virus A and influenza virus B is closely analogous to the difference between type I and type II pneumococci. The disease produced is pathologically similar, but immunologically unrelated. An attack of influenza B is indistinguishable from the more frequently observed influenza A; but the antibody produced in convalescence is quite distinct. The serum will then neutralize influenza virus B, but there is no increase in antibody against influenza virus A above the amount initially present. Epidemiologically, there is evidence that influenza virus B differs from influenza virus A in being less prone to produce sharp epidemics and more inclined to smoulder sporadically during the winter (Taylor *et alii*[7]). It can on occasion, however, produce perfectly typical epidemics.

For those who have no direct interest in the technical side of bacteriology, one can summarise the position by saying that technical methods for the study of epidemic influenza are now as well established, and in a properly equipped laboratory as readily applicable, as the standard bacteriological procedures used in the study of diphtheria or typhoid fever. Superficially they may appear different; but they are equally capable of supplying the data needed for understanding and eventual control.

Recent Incidence of Influenza in Victorian Camps.

To give some idea of the part played by virus influenza in the general group of respiratory infections, the conditions last year and this year in Victorian camps, as revealed by the application of these methods, may be described. In 1942 the dominant feature was a sharp epidemic of influenza A, arising in the last week of April and disappearing before the end of June. In July there was a high incidence of respiratory infection; but no evidence of either A or B influenza was obtained at this period. It is of considerable interest that among American troops in camp in Victoria no evidence of the May-June epidemic of influenza A was obtained, but a sharp rise in incidence occurred in July, presumably owing to the same non-influenzal infection prevalent at that time in Australian troops. In 1942, then, we have a sharp influenza A epidemic of six weeks' duration superposed on a fairly heavy winter incidence of non-specific infections. Some of the latter may have been due to influenza virus B, but none were proved so.

This year the incidence of upper respiratory tract infections in the camps has been moderate, with no suggestion of a typical influenzal epidemic. Nevertheless, we have isolated four influenza virus A strains and one influenza virus B strain, as well as obtaining immunological evidence of four more A and two more B infections. The results obtained from the study during June of nine patients in hospital in a northern Victorian camp express the position very clearly (Table I). It will be seen from Table I that of nine patients, all showing essentially similar symptoms, one was proved to be infected with influenza virus A and one with influenza virus B, while the other seven gave no evidence that either virus was responsible for the condition. At the end of May a small camp epidemic amongst troops recently returned from the north was apparently due mainly to influenza virus A. The two other B virus infections were found during July in soldiers from different areas. With these exceptions, all other tests made have given no evidence of influenza virus infection.

The position this year is, therefore, that there has been an incidence of "U.R.T.I.", which includes at least three ætiological types, influenza A and B, and "unknown", the last forming much the largest group. Findings of this sort have been made previously, for example, in England during 1939—and they present a difficult problem in epidemiology. The influenza A infections probably represent the mopping up of small pockets of susceptibles who for one reason or other escaped the epidemic in the previous year. The epidemiology of influenza B infections in Australia is still unknown; this is, in fact, the first reported isolation of this virus in Australia. The big group of clinical influenzas not grossly distinct in symptoms from proved virus A or B infections, but giving no hint from laboratory investigations as to their ætiology, remains a puzzle and a challenge. We have made some strenuous attempts to answer the challenge; but results so far are wholly negative.

TABLE I.

Results of Investigation of a Group of Nine Men with Respiratory Infection during June, 1943.[1]

Patient.	Serological Test.				Isolation of Virus.
Fo	A	+++	B	−	A
Fl	A	−	B	−	
L	A	−	B	−	
M	A	−	B	−	
D	A	−	B	−	—
T	A	±	B	++	B
N	A	−	B	−	
R	A	−	B	−	—
S	A	−	B	−	

[1] Serological tests were made by Hirst's haemagglutination method, antibody titres during illness and two weeks later being compared and the rise, if any, indicated. Virus isolations were made from throat washings (often pooled from two or more patients), which were filtered through gradocol membranes and inoculated into chick embryos by the amniotic method. Brackets indicate pooling of throat washings. Thus the influenza A strain was isolated from the pooled washings of the first four patients. Its isolation indicates only that one or more of the four patients was infected with the virus.

The Pathogenesis of Influenza.

Influenza is a typical droplet infection contracted by the inhalation of droplets of saliva containing the virus or of the dried flakes which result when such droplets evaporate. Experiments with ferrets have shown conclusively that air-borne transfer of the disease in this fashion can occur, and there is no reason to think that other methods of infection are of any practical importance among human beings.

The virus is deposited normally in the nasal mucosa, and if infection is to occur it will commence in the respiratory epithelium of the nasal cavity. All experimental work and all clinical experience is in agreement that the primary infection is strictly limited to the epithelium of the respiratory tract—nasal, laryngeal, bronchial and bronchiolar. The virus can multiply only within living cells of this particular system, and the essential damage produced is a more or less widespread necrosis of the epithelium, with secondary inflammatory changes. The exact distribution of this epithelial damage in human influenza is by no means certain. Patients suffering from simple influenza do not come to the autopsy table, nor are they subjected to detailed bronchoscopic study, so that deductions can be made only from symptoms and from analogy with experimental infections. In the monkey I have found (Burnet[8]) that severe damage is almost wholly limited to the bronchioles—that is, those parts of the bronchial tree which have no cartilaginous support—and there are indications that this section is also of great importance in the human infection. Severe influenza nearly always produces clinical and radiological evidence of bronchiolitis, and this may well be the principal lesion of all those typical cases of influenza in which nasal symptoms are (initially, at least) almost absent. The human nasal mucosa is undoubtedly susceptible to influenza virus. In one of the subjects whom I have experimentally infected with moderately virulent influenza, acute nasal symptoms preceded the onset of general symptoms by about eighteen hours, and there have been a few instances of fairly acute rhinitis amongst the many subjects to whom we have administered attenuated virus.

During the 1918-1919 pandemic, a few subjects came to autopsy in whom no evidence of secondary bacterial infection was present (Goodpasture[9]). It is reasonable to regard the death of these patients as due to the onslaught of the virus itself. Histologically, necrosis or desquamation

of all the respiratory epithelium down to the alveoli and including the trachea and larger bronchi was found. The symptoms of the hyperacute form, with its characteristic heliotrope cyanosis and the pathological picture, both reminded wartime observers of the results of chlorine or phosgene gas poisoning. Essentially the lesions were probably similar—a rapid necrosis of the respiratory epithelium with widespread exudation of inflammatory fluid. In the one case the agent was an irritant gas, in the other a hypervirulent pneumotropic virus flashing almost explosively over the whole of the susceptible epithelium. It is highly probable that the severity of an influenza epidemic is primarily determined by the speed with which the primary infection spreads over the respiratory linings and by the actual extent to which these surfaces are involved.

In fact, we could probably account for most of the differences amongst the whole group of primary respiratory tract infections by variations on this one theme of superficial epithelial damage. The intensity of damage to the individual cell, the speed with which the infection spreads over the respiratory tract surfaces and the extent of the area involved, all are more or less directly correlated. As the vigour of the virus concerned increases, we have decreasing local and increasing general signs and a progressively greater antigenic stimulus. These differences, *plus* the effects due to the largely accidental association of bacteria, give rise to the multiform picture of upper respiratory tract infection, from the simplest cold to the rapidly fatal "pneumonic" influenza.

The part played by bacteria in these infections is for the average practitioner of much more importance than the relatively innocent primary virus disease. At every level secondary bacterial infection may occur, though its extent and seriousness may, of course, vary greatly. The primary factor favouring this bacterial invasion is the epithelial damage with loss of the efficient protective mechanism based on the ciliated epithelial cells. This mechanism consists essentially of a thin, continuous sheet of mucus supported on the tips of the cilia, which move it constantly toward the throat or anterior nares. Underneath the mucous film is a serous fluid bathing the cilia. This fluid is rich in lysozyme and contains small amounts of serum antibody. This combined chemical cleaning mechanism is put out of action by the virus, and proliferation of any pathogenic bacteria that may be present is correspondingly favoured. The various types of acute and subacute bacterial damage that may follow primary virus infection of the respiratory tract are both familiar and important; but their consideration lies outside my field, and I shall make no attempt to discuss them.

The Control of the Respiratory Tract Infections.

It is a commonplace that civilized communities have been able to prevent, more or less effectively, practically all types of infectious disease except those spread by the respiratory route. Any discussion of the control of such diseases must therefore be more a consideration of possibilities than one of established successes.

There has been considerable recent discussion on the possibilities of preventing respiratory infections by methods fundamentally similar to those that have been so successful in preventing the intestinal diseases—that is, by preventing transfer of infection from the patient or carrier to susceptible subjects. For the intestinal diseases this is essentially a matter of efficient plumbing; for the respiratory tract diseases it calls for some means of rapid air sterilization, so that droplets are rendered harmless before they are inhaled by any susceptible person. This can be done for certain special purposes by one of two methods: either the air can be drawn away from the point of contamination and passed through a region heavily irradiated with ultra-violet light before being recirculated, or an adequate concentration of some antiseptic substance may be maintained in the air, either in the form of a mist (aerosol) or as an actual vapour. The vapours of propylene glycol and one or two related compounds are the most effective of those so far tested against influenza virus.

I do not think that these methods are likely to be of the slightest practical significance in regard to the general problem. They may be valuable in operating theatres, and some work suggests that they can be applied in school rooms with beneficial effect. In one well-controlled experiment (Wells, Wells and Wilder[139]) the spread of measles, mumps and chicken-pox was significantly reduced in the school rooms fitted with ultra-violet sterilizing lamps; but it is interesting to find that there was no effect at all on the incidence of colds. The ordinary person cannot possibly carry out all his social activities in a sterilized atmosphere, and it would probably make little difference to the incidence of influenza if theatres and other places of indoor crowding were equipped in this way.

As in every problem of epidemiology, we must bear in mind the principle that it is justifiable to attempt to eliminate a microorganism completely only when circumstances are such that the measures required can be continued indefinitely. If the influenza virus were successfully removed from a large community for five or ten years by any means whatever, one could be absolutely certain that any breakdown in the method of prevention would result in a sudden almost universal epidemic as soon as the virus was reintroduced into the community.

When a pathogenic microorganism has to be accepted as a permanent part of the biological environment, there are four main ways by which its harmful activities can be reduced. The first is by ensuring that children are adequately nourished and in good health when they first come into contact with the microorganism, so that they make a good start in developing the acquired immunity which, with recurrent stimuli, they will carry through life. The second is by imitating the natural process of immunization by some artificial means (toxoid immunization against diphtheria is the classical example), so avoiding the accidents associated with the natural process. The third is by short-term passive protection in the presence of any abnormal activity of the microorganism; this may be by the use of immune serum or occasionally by administration of some chemotherapeutic agent. Finally, we have the possibility of treating the developed disease by whatever specific remedies are available.

It is by developments along these lines that control of the respiratory infections must be looked for. In the discussion of such methods it will be advisable first to say something about the evidence as to the extent of the immunity which follows infection by the respiratory viruses. According to Dochez, immunity to the common cold is almost non-existent. Chimpanzees could be reinfected as early as four weeks after recovery from a typical cold, and if we accept the American figures that on the average most people have about three colds a year, nearly always in the colder seven months, then the average duration of immunity must be less than three or four months. In isolated Arctic communities like those of Spitzbergen and northern Greenland, there is a well-known almost universal incidence of colds following the arrival from overseas of the first ship of the summer. The most likely interpretation of such findings is that in normal community life there is a constant circulation of respiratory pathogens including the virus or viruses of the common cold, that both clinical and subclinical infections are repeatedly taking place and maintaining a moderate grade of immunity, and that clinical colds result when the appropriate climatic factors, the presence of a slightly more active virus than usual and a low individual immunity, coincide.

If this interpretation is correct, little is to be gained by seeking a method of artificial immunization against colds. If natural immunity is so short-lasting and inconstant, artificial attempts are likely to be even more so. Any approach to the prevention of colds must be along other than immunological lines.

With influenza, the position is a little more promising. It must be rare for anyone to have two attacks of true virus influenza in a single epidemic, and no such instance has been reported in the literature. After an attack there is a rapid increase in the amount of antibody in the blood, followed by a fall, at first rapid, then slowing, and the

antibody usually persists for a year or more at a level above that before infection. Several experiments with volunteers, including one described by Miss Foley and myself,[10] have shown that susceptibility to experimental infection with moderately virulent influenza virus is closely correlated with a low level of circulating antibody. It is therefore reasonably certain that an influenza epidemic normally burns itself out when a sufficiently large proportion of those initially susceptible have been infected, have developed antibody and concomitant immunity, and so have been transferred to the "non-susceptible" category.

The time at which a person convalescent from influenza again becomes susceptible to infection by the same type of virus probably varies greatly from one individual to another. At least four instances are on record of persons suffering second attacks of influenza A two years after the first attack. From epidemiological evidence, it seems likely that most persons develop an immunity that has some protective effect for two or three years, but that a considerable proportion (perhaps 10% to 20%) have lost their acquired resistance completely within two years. These statements refer to the normal type of influenza, such as has been experienced during the last ten years. With regard to the hypervirulent influenza of the 1918 type, there was very little evidence that immunity lasted more than a month or two. Conversely, when artificial infection experiments on human beings are made with strains more or less attenuated by laboratory passage, a moderate degree of resistance induced some years previously may be sufficient to prevent infection. It is a reasonable suggestion, supported, however, by only one little shred of evidence (Rudd[12]), that in the early stage of an epidemic only persons with low immunity are attacked. As the epidemic gathers force a higher degree of immunity is needed to give protection.

As it is known that substantial immunity against influenza can be produced in laboratory animals by various types of artificial immunization, it is natural that much work has been directed toward providing a method for human immunization. We might safely assume on general grounds that a satisfactory method of artificial immunization would provide an immunity approaching in effectiveness the average degree of immunity which follows a natural symptomatic infection; but we could certainly not expect it to produce any greater immunity. In general, we could hope that immunization carried out in autumn would provide a substantial resistance to any epidemic occurring during the same winter; but we could prophesy with some conviction that it would have no significant effect in subsequent years. So far, the net result of five years' extensive work on the problem, particularly in the United States of America, has been disappointing. In several institutional outbreaks it has been shown that recently immunized subjects had about a 50% advantage over the unimmunized controls. In at least an equal number of other experiments, no difference in susceptibility between immunized and control populations was observed. However, progressively more effective immunizing vaccines are being prepared, and I think results are likely to be better in future.

This is not the place to discuss technical details of immunization against influenza, and I shall give only a brief account of the current methods. There are only two principles involved. In one type of immunization the aim is to give one or more subcutaneous inoculations of formalin-killed virus in the largest practicable dose, while in the other type living attenuated virus is administered intranasally, with the object of provoking a mild asymptomatic but immunizing infection.

In recent years all methods have found their actual immunizing material in the fluids or tissues of infected chick embryos. The most convenient form for subcutaneous vaccination is the allantoic fluid simply treated with a small proportion of formalin. There is a tendency at present to use more concentrated preparations, in which the virus is precipitated by some suitable method from the allantoic fluid and resuspended in about one-tenth the original volume. Such material given in ten times larger doses undoubtedly produces a greater rise in antibody level; but whether there is a corresponding improvement in protection against influenza has yet to be proved.

The principle of the method is simply to introduce a large amount of antigen into the body and induce a rise in the level of antibody in the blood. The protection given is based on the liberation of small amounts of serum antibody into the fluids secreted on the respiratory mucosal surfaces. The experiment by Stokes and Henle,[13] in which children previously immunized in this fashion were sprayed with a moderately virulent living virus, gave quite strikingly favourable results. In the control group, ten infections occurred among 28 children (35%), but only one clinical case occurred amongst 44 immunized children. There are, however, good reasons for believing that their test strain was probably inferior in infectivity to an actual epidemic strain, and no results so satisfactory as these have yet been recorded in the field.

The second method of intranasal immunization was first tried by the Russian workers Smorodintseff *et alii*[14] and has been extensively developed in my laboratory. Here again the principles involved are simple. By growth in a foreign host—in this case, the chick embryo—the virus becomes attenuated for its natural host, man. The attenuation can be pushed to such a point that no effect whatever follows its intranasal administration in volunteers, neither symptoms nor immunity response. For immunization an intermediate level of virulence is needed, which in the vast majority of subjects produces no general symptoms and only trivial local ones after intranasal administration. In a small proportion of the most susceptible "one day influenza" with definite general symptoms may be produced.

Intranasal administration of such attenuated strains is intended to provide an imitation of the process by which subclinical infection frequently occurs during an epidemic. The virus multiplies in a natural site, provokes a general antibody response and may also be expected to provoke any local changes which may play a part in immunity. In our work along these lines we have shown that a large proportion of persons with an initially low antibody level respond with a rise in antibody level and with an increased skin reactivity, which may indicate the development of some degree of local immunity in the nose. In one experiment Miss Bull and I[15] showed that three to six months after immunization nearly all the subjects tested again with the same type of virus (B strain) failed to yield a second antibody response; this indicated a persisting resistance to reinfection.

We have, however, so far failed to obtain any valid evidence as to the effectiveness or otherwise of the procedure in giving protection against influenza. As nearly all investigators have found, it is a difficult matter so to arrange things that an immunized and a statistically valid control group are both exposed to a sharp homogeneous epidemic of influenza at the appropriate time. The irregularities of incidence in different groups, and the frequent occurrence of infections not due to influenza virus, but clinically similar, make any trials without alternate experimental and control subjects quite useless as a test. Last year the evidence we were able to collect suggested that the effect had been beneficial, but only to a limited extent, in the influenza A epidemic of May and early June. This year about 20,000 men were treated alternately with A and with B attenuated virus, on the theory that if an A epidemic appeared those immunized with B would serve as controls and *vice versa* if a B epidemic arose. To date no epidemic has occurred in the camps; but there has been a moderate prevalence of respiratory infections in which are included a few A and a few B infections; the great majority of subjects showed no evidence of either type of influenza virus. Unless a definite epidemic of influenza of one type or another occurs later, no conclusions whatever will be possible.

Such difficulties are commonplaces of influenza research, depending essentially on our inability to forecast the future of the most elusive of all epidemic diseases.

From the practical standpoint one can make two pronouncements. The first is that a large proportion of the winter respiratory and pharyngeal infections are not

influenzal, and are due partly to viruses not yet isolated, partly to bacterial pathogens. No immunological approach to these is yet possible. In the second place, it can be stated that in a clear-cut epidemic of virus influenza, the evidence suggests that immunization of susceptibles by either of the methods described will reduce the incidence to a moderate degree; but no method has yet been conclusively proved to be effective, and the most that has been claimed is a 50% reduction in morbidity. Such a moderate degree of success may conceivably make it worth while to immunize large groups of persons engaged in important work; but it is hardly sufficient to suggest that immunization would be worthy of general application. One would stress particularly that the most efficient influenza vaccine would probably be quite useless to the person who "gets influenza every winter".

In the third place, the major problem of preventing or minimizing the onslaught of a pandemic of 1918 character has not yet been visualized. There is some reason to hope that if the virus responsible was of known antigenic type it might be possible to produce a basic immunity by appropriate immunization, which, though it would probably not give protection against infection, might well prevent a fatal outcome. The possibility of providing such help in the event of a serious pandemic is the main justification for current influenza research.

I shall deal only briefly with the two final headings in the list of ways by which influenza may be combated. In the sphere of passive protection the Russians (Smorodintseff *et alii*[32]) claimed to have achieved striking success by allowing persons exposed to an epidemic to inhale considerable amounts of immune serum in the form of a mist. In theory at least, the antibody is retained on the susceptible mucous membranes in effective amount for about a fortnight and there blocks the initiation of infection. The only reported experiment produced a 90% reduction of incidence in the treated as compared with the control series. Until these experiments are repeated, the Russian results should be treated with reserve; but it is by no means unlikely that some modification of this method may become the best practical method of protection against influenza. It has the great practical advantage that the administration of the serum is carried out when the existence of an epidemic is recognized, not like vaccination methods, some time before an expected epidemic, which may well fail to materialize. I understand that arrangements to test the effectiveness of this method of passive protection had been made in England and probably in the United States last winter, but no epidemics appeared in either country. If results in the next epidemic are favourable, there is likely to be a considerable reorientation in the outlook on prevention of influenza.

Finally, there is the possibility that a specific chemotherapeutic agent will be discovered and will render all immunological methods obsolete. All that can be said at present is that extensive tests in England and America with hundreds of compounds have failed completely to uncover any substance with the slightest promise of therapeutic value against influenza virus infections. At the risk of being proved wrong in the next batch of journals from overseas, I should think it unlikely that any agent acting on the same general principles as the sulphonamides will be developed against the typical viruses.

If a pandemic of 1918-1919 type should reappear, it will be a matter of major human importance to know whether the fatal outcome is essentially due to bacterial action and hence to be prevented by sulphonamides, or whether the damage due to the virus is itself sufficient to cause death. In the latter case no chemotherapeutic agents at present known would be of any value.

Conclusion.

This abbreviated account of an enormous subject must end therefore on a rather pessimistic note. A great deal has been learnt about influenza and the related infections; but there is no clear indication that any really practicable method of preventing it is likely to be developed in the near future. If it were merely a question of dealing with the relatively minor varieties of winter ailments that we meet every year, there would probably be little call to do anything beyond make an attempt to improve general health by attention to nutrition and environment. But with the experience of 1918-1919 behind us, and with the certainty of human disorganization in Europe and Asia at least equal to that of 1918-1919 ahead of us, research on influenza must go on. Somehow we must be ready to prevent the mortality of such a pandemic—a mortality which, like that of war itself, strikes mainly on young adult populations. That is the main human justification for continued research on influenza and its relatives.

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Reports of Cases.

A CASE OF INFANTILISM WITH GOITRE, DIABETES MELLITUS, MENTAL DEFECT AND BILATERAL PRIMARY OPTIC ATROPHY.

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Marrying their cousins, nay their aunts and nieces,
Which always spoils the breed, if it increases.

—LORD BYRON, "Don Juan", Canto I.

THE doubtful truth of the foregoing statement will be discussed as this report proceeds.

CLINICAL RECORD.

The patient, R.N., a male, aged eighteen years, was admitted to the Royal Prince Alfred Hospital with *diabetes mellitus*, from which he had suffered for ten years. He complained also of poor vision in both eyes, for "as long as he could remember". The onset of the diabetes was quite typical, with polydipsia, polyphagia and polyuria; dietetic and insulin treatment was instituted and the symptoms were relieved. Of late, the patient had been having attacks of giddiness and dizziness, relieved by food. In hospital these were found to be due to hypoglycæmia. The blurred vision, worse in the left eye, was such that the patient stated that he could see a small object only if it "was held up close to his face and moved about". The patient had no other complaints about his health.

The onset of the defect in vision appears to have been earlier than that of the diabetes, and the blurring does not appear to have become worse in the last few years.

On examination, the patient appeared physically and mentally younger than his stated age. His weight (five stone nine pounds) and height (four feet eleven inches) were well below the average for a male of eighteen years (Davenport), and were in the vicinity of those of a child of twelve to fourteen years (Faber). The voluntary musculature was poorly developed (see Figure I, postural hypotonia). Neither adiposity nor skeletal deformity was present.

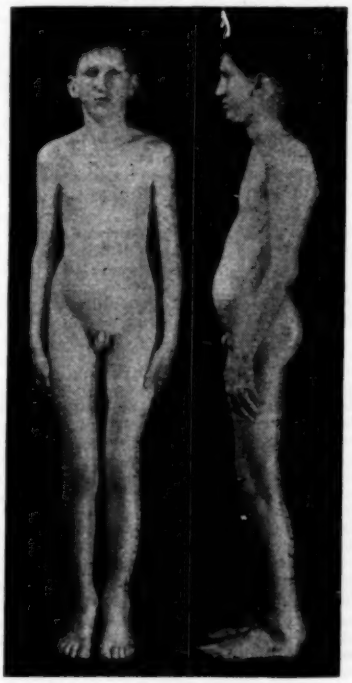

FIGURE I.
R.N., aged eighteen years. Note infantilism, genital hypoplasia, goitre and postural hypotonia.

The thyreoid gland was smooth, soft and symmetrically enlarged (Figure II). There were no pressure effects. The basal metabolic rate was +1% (normal). Microscopic examination of biopsy material revealed flattening of the alveolar epithelium, some increase of interalveolar connective tissue and infiltration with small round cells; that is, the gland showed some degree of involution, although it maintained function adequate for present needs. There was no other evidence of hypothyreoidism.

The bone age (as indicated by radiological examination of the epiphyses) was normal.

The penis and testes were very small; the testes had descended into the scrotum. There was no appreciable growth of pubic or facial hair. Operations for congenital bilateral inguinal hernia had been performed in early infancy. Psychically, the patient had never had any heterosexual interests.

Deficiency of internal secretion of the pancreas was indicated by glycosuria, diminished sugar tolerance and the associated features of *diabetes mellitus*. Stabilization of the condition on a 1,600 Calorie diet could be effected by the daily hypodermic injection of 30 units of insulin. No evidence could be found in the stools of deficiency of the external pancreatic secretion.

Radiologically, the pituitary fossa was small in size, but normal in shape and contour.

The patient's mental age, estimated by the Binet-Simon test (revised by L. M. Terman[18][19]), was twelve years, and by the Porteus maze test it was twelve and a half years. The intelligence quotient is thus in the vicinity of 75%, and the patient may be regarded as mentally backward, but not quite feeble-minded. Emotionally, the patient was unstable; he cried easily on slight provocation. His mother stated that at home he was wayward, difficult to manage and obstinate; he would refuse to keep to his diabetic dietary and insulin, and would fly into a tantrum and weep when she persisted in making him do so.

Ophthalmoscopic examination revealed the presence of considerable pallor of both optic disks, with atrophic cupping; the *laminæ cribrosæ* were clearly visible. The margins of the disks were sharply defined (primary optic atrophy). A large patch of degeneration was visible at the left macula. There were no hæmorrhages and no white patches, and there was little resemblance to diabetic retinitis. Examination of the visual fields disclosed a small central scotoma in the left field and a slight nasal indentation; the right field was fairly normal. The visual acuity was poor; it was approximately $^{6}/_{36}$ in the right eye and $^{6}/_{60}$ in the left eye. No marked error of refraction was found. No other neurological abnormality was found. The patient had never suffered from epileptic fits.

No clinical abnormalities were found. The Wassermann and other laboratory tests produced normal reactions.

In summary, it may be stated that the patient was suffering from general physical and mental retardation, from defects in the thyreoid, sex, pancreatic and pituitary glands, and from bilateral primary optic atrophy.

FIGURE II.
R.N., aged eighteen years. Note the enlarged thyreoid gland.

Family History.

The patient and his siblings are the children of a first cousin marriage. A sister, aged nineteen years, is apparently normal according to the mother.

Another sister, aged twelve years, has suffered from *diabetes mellitus* since the age of three years, and from epileptic fits since the age of four; she has had poor vision since the age of ten. On examination, her weight (five stone nine pounds) and height (four feet eight inches) were found to be within the range of normality according to the standard height-weight-age tables of Faber. There was no enlargement of the thyreoid gland. Examination disclosed pronounced primary atrophy of both optic disks.

A brother, aged five years, has also suffered from diabetes since the age of three years, and from epileptic fits since the age of four years. On examination, his weight (three stone three pounds) and height (three feet eight inches)

were found to be within the range of normality according to standard height-weight-age tables of Faber. There was no enlargement of the thyreoid gland. Examination of the optic disks revealed some pallor, more pronounced on the right side.

The mother, aged forty-three years, is apparently normal. Her general development is normal; her height is five feet five inches and her weight ten stone four pounds; no enlargement of the thyreoid gland is present. Her vision is good and her optic disks are normal. Two of the mother's sisters have had operations for goitre, but otherwise seem normal.

The father, aged forty-five years, is apparently normal. The father's brother had suffered from epilepsy since he was a child, and died in an attack of *status epilepticus*.

The maternal grandparents are not known to have presented any abnormality.

Various abnormalities were reported in connexion with the paternal grandparents. The female grandparent was confined to an asylum after the age of sixty years; she was psychotic. The male grandparent behaved strangely; he used to strip off his clothes and wander about, and was possibly psychotic. (See Figure III, the family tree.)

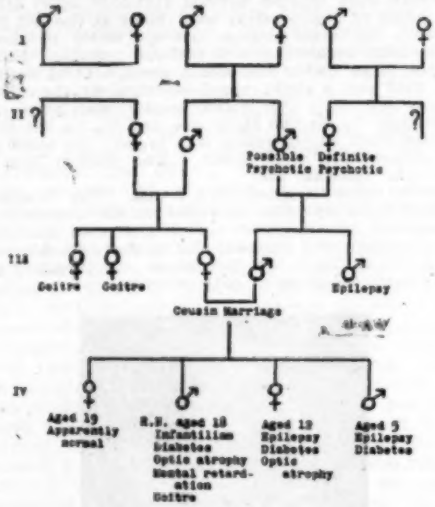

FIGURE III.

I: Great-grandparents; no details of abnormality available. II: Grandparents. III: Parents and their siblings. IV: R.N. and his siblings.

Habitat.

The patient and his immediate relatives live in the Muswellbrook area. This is one of the well-marked regions of endemic goitre in New South Wales. In an investigation of these areas, the results for Muswellbrook were as follows:

> Girls: 1,127 with moderate thyreoid enlargement; 556 with severe thyreoid enlargement.
>
> Boys: 550 with moderate thyreoid enlargement; 163 with severe thyreoid enlargement.

These figures are per 10,000 of population (Harvey Sutton, 1927).

DIFFERENTIAL DIAGNOSIS AND DISCUSSION.

The Dwarfism and Infantilism.

In dwarfism, growth in stature is stunted, but the adult sex characteristics, mental and bodily, are present. By infantilism we mean smallness of form; but also the modelling of the bodily regions is imitative of childhood, and the onset of sexual development is delayed. The patient, R.N., clearly suffers from infantilism, and its differential diagnosis will now be discussed.

Secondary Infantilism.

There was no evidence that the infantilism was secondary to syphilis, cœliac disease, congenital heart disease or renal disease, ankylostomiasis, bronchiectasis or other such chronic affection. Nor was the infantilism considered to be a secondary nutritional defect due to vitamin lack, or to deficiency of external pancreatic secretion. There was no evidence of mongolism.

Infantilism due to Hormonal Deficiency.

Thyreoid Deficiency.—None of the features of cretinism was present. The enlargement of the thyreoid and the microscopic appearance of the gland are compatible with endemic goitre, and the patient is known to have resided in an endemic goitre area. On this point, Harvey Sutton[15] makes the following statement:

> In school children enlargement of the gland is associated with good health; they are usually bright and above the standard weight for height. The incidence is well distributed throughout the population and no association with previous illnesses is noted.

The patient's basal metabolic rate and bone age were normal, and it was concluded that the goitre was of little importance in the genesis of the patient's condition.

Gonadal Deficiency.—The sexual development was defective; but the patient had neither the height nor the bodily configuration of eunuchoidism; his upper and lower bodily measurements were approximately equal and the time of epiphyseal closure was normal.

The Pancreas.—There was no evidence of deficiency of the external secretion of the pancreas. With regard to the internal secretion, Boyd and Robinson[3] report the case of a boy, aged nine years, who had suffered from *diabetes mellitus* since the age of two years. He was an emaciated dwarf, unable to utilize any carbohydrate. Much recovery ensued following a year of insulin treatment. Against the suggestion that R.N.'s retardation may be due to the diabetic condition are the following facts: (i) the institution of insulin and dietary treatment at an early age and probably close to the onset of the disease; (ii) the presence of marked, defective development of the testes and the associated bilateral, congenital inguinal herniæ; (iii) the circumstantial evidence of a small pituitary fossa; (v) the presence of mental backwardness.

Progeria.—The patient's clinical picture presented no resemblance to progeria.

Pituitary Defect.—The pituitary fossa was small. The patient's appearance showed no resemblance to Brissaud's or Fröhlich's types of pituitary infantilism, in that no adiposity was present. Some features of the Lorain-Lévy type of pituitary infantilism, however, were noted—namely, skeletal unudergrowth, with no great disproportion of parts, genital hypoplasia, and the absence of obesity. Mental retardation (present in R.N.) is not, however, a feature of the Lorain-Lévy type of infantilism. The hypogenitalism may be considered to be primarily gonadic or due to deficiency of gonadotrophic hormone; but the epiphyses appear to be closing at the normal times. In this respect the infantilism is more like that due to developmental defect. The diabetes may be primarily of pancreatic origin or due to pituitary defect. If it is of pituitary origin, it may be due to excess of the diabetogenic hormone, or to deficiency of pancreotrophic hormone. Thyreoid disease by itself does not cause *diabetes mellitus*. Economy of hypothesis may suggest a pituitary origin for the hypogenitalism, diabetes and defective growth (deficiency of growth hormone); but this may be a false simplification, and as has just been pointed out, there are certain features which do not fit in completely with this view.

Résumé and Interpretation.—A purely endocrine interpretation would be as follows. There is a more or less normal thyreoid secretion in the presence of endemic goitre; the growth hormone of the anterior pituitary gland is deficient, and possibly an associated lack of gonadotrophic secretion is causing hypogenitalism; the *diabetes mellitus* is due either to primary pancreatic defect or to secondary to anterior pituitary (pancreotrophic hormone) deficiency. Perhaps deficiency of thyreotrophic hormone made the patient more liable to develop endemic goitre. Some resemblances to the Lorain-Lévy type of pituitary infantilism were noted; but against this diagnosis was the mental retardation and the normal time of closure of the epiphyses. Because of the last-named discrepancies and in view of other findings, it seems more likely that the patient's condition may be due to developmental defects, probably of genetic origin, giving rise to effects not all of which are mediated by changes in the endocrine glands.

The Ocular Changes.

The patient also suffered from bilateral primary optic atrophy and left macular degeneration, presenting a picture quite unlike that of diabetic retinitis. No toxic cause could be assigned to the atrophy. There was no evidence of previous optic neuritis. Examination of the visual fields disclosed no bitemporal hemianopia, and there was no radio-

logical or clinical evidence of any intracranial pathological condition. The presence of poor vision in the patient's twelve-year-old sister introduced the possibility of Leber's familial optic atrophy. The distinctive features of the Leber's syndrome are as follows: (i) bilaterality in the acute stage; (ii) the frequency of absolute scotomata in the chronic stage, often symmetrical, though occasionally irregular; (iii) the absence of apparent infection or toxæmia; (iv) failure of recovery; (v) hereditary and familial character, males being usually, although not exclusively, affected; (vi) onset at or about puberty. The ætiology is obscure; the condition has been regarded as an abiotrophy of optic neurones (Rehsteiner). On the other hand, J. H. Fisher[9] assigns the cause to a temporary pressure on the optic chiasma by the pituitary gland, which enlarges about puberty. He states that in cases of tumours of the chiasmal region, central scotomata often precede the development of bitemporal hemianopia, and postulates that a disturbance of the pituitary of a temporary character and moderate degree could adequately explain Leber's optic atrophy, in which the inherited tendency would not lie in a special vulnerability of the macular fibres of the optic nerves, "but in a liability of the pituitary to such a limited disorder as I here suggest".

In R.N.'s case, the associated pituitary defect could possibly support Fisher's views if the optic atrophy was of the Leber type; but this does not appear to be so. The age of onset was too early, symmetrical scotomata are not present and there was no history of visual defect in the previous generation, although the condition appears to be familial, the patient's sister being also affected. Further, the evidence would point to the pituitary's being smaller than normal in this case. The chief difficulty in regard to Fisher's paper, according to Kinnier Wilson,[20] "was that he transferred the defect from the optic nerve to the pituitary body". So far as Kinnier Wilson was aware, "bitemporal hemianopia has never been recorded in the affection (Leber's optic atrophy), while inherited defect of the pituitary seems unknown".

Conclusions.

No adequate cause could be found for the patient's primary optic atrophy, and no relation could be assumed between it and changes in the pituitary gland, which, if present, would appear to be a separate condition. On the other hand, the alternative is that all the abnormalities are neuro-endocrinal effects which may be accounted for by developmental defects of genetic origin.

The Significance of the Cousin Marriage.

The common impression that marriages of cousins are frequently followed by insanity, amentia, mutism, deafness, visual and other defects is supported by many pedigrees. "On the other hand, the opposite often occurs, as would be expected, when the stock in question is a sound one with qualities above the average—the Wedgewood-Darwin-Galton group of families is a famous instance. Inbreeding intensifies whatever qualities, good or bad, the stock possesses" (Eldon Moore[12]).

Inbreeding tends to produce an increase in the proportion of factors in the homozygous state, and a decrease of those in the heterozygous condition. The great risk of consanguinity is that undesirable characters of varying degrees of recessivity, hitherto latent and hidden in a heterozygous stock, are rendered homozygous (present in double dose) and so brought to the surface as manifest abnormality. No one can possibly know the whole genetic complex of any organism, and inbreeding occasionally brings disastrous results.

Hogben[3] makes the following statement:

> There is probably an enormous number of factors for defects of development; the possibility of a person carrying any given one of these is remote, but the likelihood of carrying at least one in the heterozygous condition is not inconsiderable.

If the patient's family tree is studied, it is seen that his antecedent stock shows morbid defects—one definite psychotic, one possible psychotic and one definite epileptic, on the father's side. The two cases of goitre (almost certainly endemic goitre) on the mother's side are of less significance. It is for just such a neuropathic stock that consanguineous marriage is fraught with risk. The incidence of *diabetes mellitus* in three of the four children, and of epilepsy and visual defect in two of the four, is very suggestive of inherited tendency. The epilepsy in the paternal uncle and its reappearance in two of the children are particularly significant. Further, the epilepsy is present in the uncle, but not in the parents. It would be difficult to explain its appearance in the children on Mendelian lines unless a recessive factor came from each parent. The cousin marriage would render this possibility more plausible. Similarly, the appearance of the visual defect and the diabetes, not known in any of the antecedents, may be due to consanguinity.

Conclusions.

We may assume either: (i) that more than one unrelated abnormality is present, or (ii) that we are dealing with a new and previously undescribed clinical syndrome. This, in turn, may be due in part at least to degeneracy produced by cousin marriage in a neuropathic stock. I incline to the latter view.

Acknowledgements.

I wish to express my thanks to Professor C. G. Lambie for his advice and encouragement, and to Mr. Woodward-Smith for the illustrations.

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NOCTUID LARVA IN THE NASAL PASSAGES OF MAN.

By H. W. S. LAURIE,
Naracoorte,

AND

H. WOMERSLEY,
Entomologist, South Australian Museum, Adelaide.

Clinical Record.

L.J.S., a male patient, aged fifty-four years, a sheep farmer, whose previous history contains nothing relevant, states that twelve months ago he commenced to have frequent headaches, with nasal obstruction and epistaxis. The headaches were frontal, and were worse in the morning and on going to bed. At night the head discomfort made him very restless. He sneezed frequently during the day.

After putting up with these symptoms for twelve months, he conceived the idea of applying tincture of iodine to his nasal passages, and, having done so, proceeded to blow his nose very vigorously. On examining the discharge on his handkerchief, he found, among blood and mucus, what he described as a "grub", which he subsequently brought for inspection. He stated that it was already dead when discharged. His symptoms have disappeared since that date.

The specimen was a larva; it was red in colour, apparently owing to the iodine, and was well preserved.

It was sent to the South Australian Museum for identification and for opinion as to the possibility of its infesting the nasal cavities of man.

Entomological Notes.

The specimen submitted for identification through the Director of the Institute of Medical and Veterinary Science, Adelaide, was identified as the probably fully fed larva of a Noctuid moth.

As received, the specimen measured 22 millimetres in length; it was entirely red in colour, the segments were somewhat contracted, and it showed no signs of maceration or decomposition. The cuticle was undamaged, and upon dissection the finer details of chætotaxy by which it was identified as belonging to the Noctuidæ could be well seen.

From the history of the case it is somewhat doubtful whether such a moth larva could have been the cause. It could hardly have lived in the tissues or passages for a period of one year unless such a habitat had retarded its growth, for such insects in this stage are plant feeders and complete their metamorphosis annually. If it had entered the passages at the beginning of the patient's illness, while he was asleep, and died there, the question arises as to whether the tissues or secretions could have preserved it over such a long period. This hardly seems possible.

The only other possibility, despite the history of the case, is that the larva may have been in the handkerchief when the patient blew his nose. Against this is the fact that the specimen was dead, and also its state of preservation and red colour.

Records of moth caterpillars infecting animal tissue seem to be few, and only the following two reports of somewhat doubtful cases have been found.

In *The Entomologist's Monthly Magazine* for April, 1941, A. N. Worden recorded the presence of a viable Noctuid larva in the subcutaneous tissues of a dog. The larva was squeezed out of a swelling in the region of the left thyreoid of a terrier bitch by bathing and compression. The swelling was apparently painless, and after release of the larva it continued to discharge serous fluid for some time. The larva was placed in a match box, where it pupated, and although the pupa failed to emerge, it was identified at the British Museum (Natural History) as that of the moth (*Antitype flavicincta* F.) the larvæ of which feed upon a variety of plants such as dock, groundsell *et cetera*. In discussing the foregoing record, T. Bainbridge Fletcher, in the same journal for May, 1941, drew attention to his own earlier record (*The Journal of the Central Bureau of Animal Husbandry of India*, Volume I, 1913, page 1) of a larva of a Cossid moth being found in the frontal sinus of a bullock upon amputation of a broken horn. Cossid larvæ are normally timber borers and live in galleries which are damp. Fletcher coined the term "setiasis" for such cases of infection by Lepidoptera.

Comment.

It seems doubtful whether a larva could exist for twelve months in the nasal cavities, either alive or dead; but the patient insists that the larva came from the nose, and the clinical record and the fact that the larva was stained with iodine would seem to support his contention.

In view of the fact that recorded cases of infestation of animal tissues by such larvæ are rare, the facts, as far as they can be ascertained, are thought worthy of record.

Reviews.

THE ESSENTIALS OF MATERIA MEDICA, PHARMACOLOGY AND THERAPEUTICS.

"THE ESSENTIALS OF MATERIA MEDICA, PHARMACOLOGY AND THERAPEUTICS" (third edition), by Dr. R. H. Micks,[1] differs from many works on the same subject, in that the author claims, with justification, "to teach the subject rather than to expound it", and to teach it with the view that the student should learn a great deal about the few important therapeutic agents rather than dissipate his efforts over a wider field of doubtful drugs.

This didactic attitude is reflected in the inclusion of revelant physiological data to introduce each section, in the original and practical therapeutic classifications, in the excellent summaries which conclude each chapter, and in the clarity of the general "set up" of the work.

Since the second edition was produced (1938) a considerable amount has been rewritten in consonance with recent advances in therapeutics, and an introductory chapter on general principles of drug action has been added. This useful addition emphasizes many aspects of drug application which, despite their importance, are often slighted. Such include, among others, variations in susceptibility and the rule of the trial dose, possible potentiation of an individual drug by synergism, and the effects of absorption and clearance rates on efficient dosage.

Among the drugs receiving fuller treatment in this edition are digitalis and quinidine, organic mercurial diuretics, the sympathomimetic amines, choline esters, and the newer anthelmintics.

Analeptic drugs are the subject of a full and critical survey. In defining them as central nervous stimulants specifically used for the purpose of reviving an unconscious patient, the author includes spinal convulsants (strychnine), sympathomimetic amines (amphetamine) and respiratory stimulants (carbon dioxide, lobeline), in addition to the cortical convulsant group (leptozol, nikethamide, picrotoxin).

A satisfying account of water balance and its relation to blood and tissue electrolytes introduces the subject of adrenal cortical deficiency and the uses of desoxycorticosterone.

In the hormone section, the mechanism of insulin action is discussed at length and the treatment of diabetic coma is featured with fullness and precision.

The chapter on vitamins summarizes all the well-established advances of recent years, but in treatment confines its observations to such avitaminoses as are known to occur in the human subject. This section also carries short monographs on hæmorrhagic diseases, naphthaquinone derivatives, heparin, dicoumarin and viper venom.

In a final chapter devoted to prescribing some brief but sound advice is given, not the least wholesome of which is an exhortation to prescribe active and powerful drugs by themselves, and to avoid meddlesome doctoring.

The book gives a refreshing sense of having been written in the atmosphere of practical bedside application rather than in the stratosphere of laboratory experiment, and, where theory and practice have not quite coincided, the author's personal opinion has the backing of sound clinical judgement and experience.

The fundamental objects of the book—to explain to the student the mode of action of therapeutically proved drugs, and to furnish practitioners with clear guidance as to their use—are well attained, and it may be recommended with confidence.

AN ELEMENTARY ATLAS OF ELECTROCARDIOGRAMS.

IN the preface to their little atlas of electrocardiograms for students and practitioners, H. W. Jones and E. N. Chamberlain remark that they consulted a philologist about the use of the words electrocardiograph and electrocardiogram.[1] His verdict was that electrocardiograph should be applied only to the instrument and electrocardiogram only to the record; it is thus in accord with the definitions of the Oxford "New English Dictionary". It is refreshing to see that the authors of a recent book which is likely to be widely read take the trouble to establish the correct usage of words which must come largely into their work: it is to be hoped that the trouble they have taken is not quite counterbalanced by the example of a leading medical journal which now prints both these words without distinction as E.C.G., nay—for even the full stops have now gone by the board—as ECG. From the fifty-two tracings in the slim atlas of Jones and Chamberlain and from the brief discussion at the beginning of each section the reader may learn to know the electrocardiograms characteristic of the important diseases and disorders of mechanism of the heart, but he will find only the barest details of electrocardiographic technique and no reference to the rarer abnormalities of mechanism or conduction. These are, of course, beyond the scope of such a book. Indeed, the frontispiece, a photograph entitled "Portable electrocardiograph arranged on a trolley", without further legend, but stated to be reproduced by courtesy of a scientific instrument company, is irrelevant and might well have been omitted. The book may be recommended to the student and to the practitioner who is new to the subject.

[1] "The Essentials of Materia Medica, Pharmacology and Therapeutics", by R. H. Micks, M.D., F.R.C.P.I.; Third Edition; 1943. London: J. and A. Churchill, Limited. 8½" × 5½", pp. 436. Price: 16s.

[1] "Electrocardiograms: An Elementary Atlas for Students and Practitioners", by H. Wallace Jones, M.D., M.Sc., F.R.C.P., and E. Noble Chamberlain, M.D., M.Sc., F.R.C.P.; Second Edition; 1943. Bristol: John Wright and Sons, Limited; London: Simpkin Marshall (1941), Limited. 8½" × 5½", pp. 56, with 53 illustrations. Price: 5s. net.

The Medical Journal of Australia

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PRIMARY ATYPICAL PNEUMONIA.

DURING the last four or five years increasing attention has been paid in the literature to an atypical form of pneumonia for which no bacterial cause can be found. The condition, which is said to be becoming more prevalent, is known by many names, and this fact alone shows that much remains to be learned about it. In bringing to the notice of readers some recent articles and discussions on the subject, we must direct attention first to the question of nomenclature. W. R. M. Drew, E. Samuel and M. Ball, all of the Royal Army Medical Corps, begin their important contribution[1] with the statement that the term "primary atypical pneumonia" is applicable to pneumonic consolidations other than those caused by any known virus, rickettsia, bacterium or chemical agent. At the same time, despite the fact that its adoption was recommended by the American Surgeon-General, they feel that the name is unsatisfactory. They think that the well-known association of the word pneumonia with a serious complaint may lead the patient to exaggerate the severity of his illness. Until the cause is discovered it is, in their opinion, unlikely that a completely satisfactory name will be found. Captain John W. Brown, of the United States Army Medical Corps, in a discussion at the Royal Society of Medicine,[2] referred to the condition as atypical pneumonia, but he gave a formidable list of names that have been used—acute pneumonitis, disseminated focal pneumonia, acute diffuse bronchiolitis, benign broncho-pulmonary inflammation, acute interstitial pneumonia, virus pneumonia. To this list he added the words "and others". At the same discussion Philip Eliman deprecated the use of the word pneumonitis because it only served to confuse the issue. H. A. Reimann, Professor of Medicine of Jefferson Medical College, who has previously written about this subject, refers to the American Army term "primary atypical pneumonia, etiology unknown" as having been adopted to avoid error, since agents other than filterable viruses may cause a similar condition.[3] As a matter of fact it was Reimann who in 1938 did a great deal to focus attention on the subject by a paper, published in *The Journal of the American Medical Association* of December 24 of that year, which will repay study today. He uses the name viral pneumonia, eschewing the ungrammatical term virus pneumonia. He insists that viral pneumonia is a syndrome and not a disease. B. E. Goodrich and H. A. Bradford write about "virus type pneumonia" and they look on it as a "distinct disease entity".

In regard to the incidence Reimann thinks that it may be only a coincidence that viral pneumonia sprang into prominence in 1938 after the introduction of sulphapyridine in the treatment of pneumococcal pneumonia, but adds that since then it has undoubtedly increased in relative and absolute numbers. Goodrich and Bradford agree that the condition is showing an increasing incidence and think that this is not to be explained alone by familiarity with the clinical concept. Reimann writes that in his experience in one year (apparently 1941) pneumonia of the type under discussion formed 15% of pneumonia among patients admitted to hospital. In a Detroit hospital the proportion was as 6 is to 7, but in the late months of 1942 viral pneumonia outnumbered pneumococcal pneumonia in his service in the ratio of 3 to 1. This may, he thinks, be partly due to the fact that patients with pneumococcal pneumonia are now largely cured at home and that only those with pneumonia that is refractory to chemotherapy are sent to hospital. J. W. Brown stated at the discussion already referred to, that at a United States Army hospital in England, of 143 patients admitted with pneumonia, 102 were suffering from the atypical form. H. Joules said that approximately 220 patients from a civilian population of a quarter of a million were admitted every year to a Middlesex hospital suffering from pneumonia. An analysis of 57 cases, seen in the preceding three months, showed that 28 were examples of true lobar pneumonia, from which a pneumococcus was obtained, 17 were typical clinically of lobar pneumonia but no pneumococcus was recovered, 12 fell into the category of primary atypical pneumonia. The condition generally runs a benign clinical course. Drew, Samuel and Ball on the basis of fifty cases observed by them among service patients describe the onset as gradual and the symptoms as including cough, headache, malaise and fever, associated with areas of consolidation in the lungs. No polymorphonuclear leucocytosis occurred, and pathogenic organisms did not predominate in the sputum; complete resolution of the lesions in the lungs took place. Reimann refers to two forms of the condition—a sporadic, non-seasonal and an epidemic or winter-month form. In the latter group he includes infections due to influenza A and B as well as unknown varieties. Other writers consider the influenzal cases as being in a different category. Reimann points out, in discussing the sporadic cases, that they were at first confused with psittacosis which they strongly resemble. He thinks it probable that the viruses of the composite psittacine group of infections, lymphocytic chorio-meningitis and the viruses established in the mongoose and cotton rat as well as others yet unknown are operative. This, as will be seen later, is a question that must be considered. Reimann states that the disease appears to be a systemic one, often accompanied by splenomegaly and nervous symptoms, in which the lungs are

[1] *The Lancet*, June 19, 1943, page 761.
[2] *Proceedings of the Royal Society of Medicine*, June, 1943, page 385.
[3] *Bulletin of the New York Academy of Medicine*, March, 1943, page 177.
[4] *The American Journal of the Medical Sciences*, August, 1942, page 163.

incidentally affected. Lieutenant-Colonel Gordon E. Heim, of the United States Army Medical Corps, stated at the London discussion that among the milder cases patients with more serious symptoms might be observed. Retroocular headache occurred, pneumonia became extensive and the respiratory rate extremely rapid, and moist rales appeared in the lungs; death appeared imminent, but recovery was the rule. Goodrich and Bradford refer to severe cases—four patients among 52 "showed an illness of critical proportions". In spite of these observations it must be noted that the illness as a rule is not severe and in most instances the patient experiences no great discomfort. In these circumstances the clinician will ask whether numbers of these infections do not pass unrecognized. The answer will have to be in the affirmative, because in many instances a diagnosis can be made with certainty only by X-ray examination. It is of interest, however, as pointed out by Drew, Samuel and Ball, that, in their series, no relation was observed between the extent of the pulmonary lesion and the severity of the cough, neither did the duration of the fever correspond with the size of the radiographic shadow. Some patients with large shadows were afebrile throughout the course of the illness. Authors appear to agree that there is no typical radiological appearance. Goodrich and Bradford state that the initial radiographic appearances may simulate those of acute exudative tuberculosis and that the study of serial radiographs may be necessary before a diagnosis can be made. As a matter of fact radiologists of lesser discernment are stated to have labelled the appearances as tuberculous, and patients are said to have been sent to sanatoria on the flimsy evidence provided by these shadows. But beyond this the differential diagnosis cannot be discussed.

The most important aspect of the subject is that of ætiology, for no real progress will be made until the causative agent has been determined. Though no single cause for primary atypical pneumonia has been discovered, there are, as Drew and his fellow workers point out, conditions characterized by similar lung changes which suggest a number of ætiological factors. They discuss the relationship to the virus of psittacosis and point out that the antibody response of the blood in some cases of primary atypical pneumonia is identical with that found in psittacosis. The psittacosis virus is widespread in pigeons in England and is possibly present in domestic animals; failure to obtain a history of contact with sick birds is, therefore, these authors hold, of little significance. That pulmonary lesions indistinguishable from those of primary atypical pneumonia can be produced in animals by many other viruses is additional evidence that this condition is caused by a virus. Drew and his collaborators refer to work on influenza and state that it has been proved conclusively that lung lesions may be caused by a virus; but all attempts to establish a relationship between the influenza virus and primary atypical pneumonia have failed. In reference to rickettsial pneumonia they refer to the work of Derrick and of Burnet on "Q" fever, published in this journal in August, 1937. What has been described as the most exhaustive study so far undertaken has been made by J. H. Dingle and other members of the Commission for the Investigation of Atypical Pneumonia and Other Respiratory Diseases.[1] The result of their search for causative agents was largely negative, but they did obtain some evidence to suggest that an unidentified agent was present in some cases. They thought that this new agent, probably a virus, was responsible for their cases of primary atypical pneumonia. Though it cannot be claimed that the ætiological role of a virus has been proved, there is every reason to hope that finality will be reached. Reimann points out that the epidemiology of this condition includes the fascinating study of the relationship and transference of viruses between animals, birds and man. The questions arise, he states, whether they are identical or whether each of the apparently related viruses are descendants of a single parent form modified by adaptation in different hosts, whether one may change into another, if each represents a specific "type" of a genus, analogous with types of pneumococci, and each type selects the host in which it is best fitted to survive. Determination of these questions would have results extending far beyond primary atypical pneumonia.

[1] J. H. Dingle *et alii*: "Primary Atypical Pneumonia, Etiology Unknown", *War Medicine*, Volume III, 1943, page 223; quoted in *The New England Journal of Medicine*, June 3, 1943, page 729.

Current Comment.

HOMOLOGOUS SERUM JAUNDICE.

It has been known for a long time that the injection of incompatible blood can cause jaundice in the recipient. The explanation of this effect is usually straightforward, though there may be difficulty in explaining some of the subtler types of incompatibility such as that which sometimes occurs between two specimens of blood belonging to the same blood group. Attention has recently been directed, however, to the fact that the injection of human serum only can cause jaundice, and can do so in such circumstances that the accident cannot be due to incompatibility between the serum and the recipient's red blood cells. It is assumed, but not proved, that this type of jaundice is due to a virus which is harmless to the donor but causes hepatitis in the recipient. The condition has been called homologous serum jaundice, and is of very great interest in view of the frequency with which serum is now given therapeutically. Certain medical officers of the British Ministry of Health have prepared a memorandum which gives a detailed account of the chief facts concerning this type of jaundice.[1] This is not really the first description of the condition, for the literature contains reports of outbreaks of jaundice for which, at the time of occurrence, there were various feasible explanations, but which appear, in retrospect, to have been due to some factor transmitted by human serum. Thus, in 1885, "humanized" lymph was used to vaccinate 1,289 persons in Bremen, and 191 of them subsequently developed jaundice; in 1937 a single batch of measles convalescent serum was given subcutaneously to 109 people in southern England, and 41 became jaundiced; more recently similar complications have occurred after the administration of small quantities of pooled mumps convalescent plasma and after the use of yellow fever vaccine containing human serum. Jaundice following inoculation with yellow fever vaccine has caused keen discussion because over 28,500 American soldiers have suffered from this complication and 81 have died as a result.[2] It is also of very great topical interest that the complication has followed the giving of massive transfusions of serum which was reconstituted from a Seitz-filtered, pooled, dried product.

The clinical picture of homologous serum jaundice is now established in main outline. The cardinal sign, of course, is jaundice, which comes on after a long latent period of sixty to ninety days. The jaundice varies in severity and, quite probably, is not an essential feature

[1] *The Lancet*, January 16, 1943, page 83.
[2] *The Journal of the American Medical Association*, Volume CXIX, 1942, page 1110.

of the syndrome. Three common manifestations are stiffness of the joints, polymorphic rashes, and enlargement of the spleen, and these serve to distinguish the disease from the closely related condition of infective hepatitis. Necrosis of the liver has been found in a few cases in which autopsies could be carried out. Further light has been thrown on the ætiology of this disease by some recent investigations of jaundice that resulted from immunization against yellow fever.[1] Nasal washings were taken by G. M. Findlay and N. H. Martin from three patients who were in the early stages of the disease, and were administered intranasally into three volunteers. Jaundice resulted in each instance, and this evidence is therefore in favour of the theory that the syndrome is due to a virus rather than to a toxin. Although this explanation is fairly satisfactory, there are certain factors which must be weighed against it. Thus there is no well-established case of homologous serum jaundice following transfusion with whole blood, and there is no instance of a person being secondarily infected under natural conditions from someone who has developed homologous serum jaundice.[2] It has recently been suggested by J. W. Bigger that the jaundice which sometimes occurs during treatment with arsenicals may be of the homologous serum type.[3] It is certain, at any rate, that the customary technique, in many of the clinics for venereal diseases, would permit the transfer of small amounts of serum from one patient to another.

THE MEASUREMENT OF OXYHÆMOGLOBIN.

A KNOWLEDGE of the hæmoglobin content of a patient's blood is sometimes of great importance to the clinician, but methods for its estimation are often unsatisfactory. Readers will therefore be interested in a short, recent article by H. F. Holden[4] in which he describes a method for the colorimetric determination of oxyhæmoglobin. The procedure which he outlines is very simple and is particularly suitable for junior workers, but it nevertheless gives results in which duplicate estimations vary over a range of only 1%. The principle of the method is that a colour produced by the oxyhæmoglobin of the blood is matched, in a colorimeter, by a colour obtained from a piece of glass. If the glass is standardized, then it is possible to state the concentration of oxyhæmoglobin as soon as one finds the depth of diluted blood which gives a colour match with the glass. Now, this principle is familiar to anyone who has used a plate of brown glass in any of the popular acid hæmatin methods for estimating hæmoglobin; but Holden's modification consists in the use of a light filter which restricts the light to the part of the spectrum that is relatively highly absorbed by oxyhæmoglobin. In this way he produces a colour which is much more stable than that of acid hæmatin, but just as easy to match. The light filter used is made of the green glass employed in railway signals. Hæmoglobin, when seen by the light that passes this filter, appears as an olive green colour, and the glass standard, of course, has to be chosen to match this same colour. If several specimens of blood are examined by this method and also by an independent method such as the standard gasometric technique of Barcroft, the glass standard can be calibrated once and for all.

Holden's interesting paper should be studied in conjunction with an article prepared as a report to the Traumatic Shock Committee of the Medical Research Council in England.[5] This article outlines some of the difficulties met with in the estimation of hæmoglobin, and gives a critical discussion of the various methods used to determine hæmoglobin values. It is pointed out that: (*a*) methods involving gas analysis give highly accurate results when used by experienced workers, but are not suitable for general use; (*b*) colorimetric measurements may be inaccurate if the standard solution is insufficiently permanent or if the blood contains hæmoglobin derivatives such as carboxyhæmoglobin, methæmoglobin, sulphæmoglobin, or methæmalbumin which give a different colour from that of the standard; (*c*) photometric measurements, in which the absorption of light is determined, are also rendered inaccurate if the hæmoglobin is partly in the form of the various derivatives detailed above, or if there is a significant absorption of light by other pigments; (*d*) estimation of the iron present in the blood corpuscles is an accurate but somewhat difficult method of determining hæmoglobin. The recommendation of this body is that the Haldane-Gowers hæmoglobinometer is the best for clinical work; but the colour standards require checking.

[1] *The Lancet*, May 29, 1943, page 673.
[2] *The Lancet*, May 29, 1943, page 683.
[3] *The Lancet*, April 10, 1943, page 457.
[4] *The Australian Journal of Experimental Biology and Medical Science*, Volume XXI, September, 1943, page 169.
[5] *British Medical Journal*, February 20, 1943, page 209.

CURE OF AN ANEURYSM OF THE SUBCLAVIAN ARTERY BY FIBROSIS.

IN 1940 H. E. Pearse published an interesting report of the experimental occlusion of the arteries of dogs by wrapping "Cellophane" around them.[1] The "Cellophane" was found to be an extreme tissue irritant and extensive changes occurred around it. The changes are described by Pearse as consisting of an intense reaction with either purulent or gelatinous fluid in the centre about which the tissue contained many phagocytic, mononuclear cells interspersed among fibrous tissue. The fibro-collagenous layer became partly hyalinized. The process caused "a steady progressive constriction of the vessel and an eventual obliteration of the lumen in some instances". Pearse thought that it was a foreign-body reaction—it was not associated with ordinary inflammation and there were very few polymorphonuclear leucocytes in the tissue. Some of the large phagocytes often contained fragments of "Cellophane". P. W. Harrison and J. Chandy, writing from Bahrain, Arabia, have reported two cases in which an attempt was made by this means to occlude aneurysm of the subclavian artery.[2] One of the attempts was successful. In the successful case the patient was a man, an old pearl diver, who was seventy years of age. He complained of severe pain in the left shoulder. The systolic blood pressure in the left arm was usually 130 millimetres of mercury and no reaction was obtained when the Kahn test was carried out. Operation was performed under local anæsthesia. The aneurysm was exposed together with more than one centimetre of normal artery on its proximal and distal sides. "Cellophane" tape which had been boiled was applied in a five-layer band both proximally and distally, and the wound was closed. The pain was unrelieved by operation and it was some time before improvement occurred. After ten months the pain had disappeared. After nineteen months the sac of the aneurysm was obliterated, the subclavian artery being interrupted by a deep groove filled with a fibrous mass. In the second case suppuration occurred and the artery had to be ligated; considerable disability resulted. Harrison and Chandy think that this method may be applicable to arteries larger than the subclavian, and even to the aorta. Whether this is true or not, the method will probably be further exploited.

[1] *Annals of Surgery*, Volume CXII, 1940, page 923.
[2] *Ibidem*, September, 1943, page 473.

REPORT OF THE REPRESENTATIVE COMMITTEE IN ENGLAND.

THE attention of members of the Branches is directed to the Supplement of the *British Medical Journal* of August 7, 1943, containing a report of the Representative Committee appointed in England by the British Medical Association in collaboration with the Royal Colleges to meet the Minister of Health in order to discuss with him the problems and difficulties involved in the establishment of a comprehensive medical service. It should be of interest to Australian practitioners in view of the discussions that are taking place in this country.

Abstracts from Medical Literature.

MEDICINE.

Gallop Rhythm.

CURTIS F. GARVIN (*The American Journal of the Medical Sciences*, June, 1943) defines gallop rhythm as a disorder of the heart beat characterized by the occurrence of three heart sounds during each cardiac cycle. He states that systolic gallop, in which the third sound occurs in systole, is rare and apparently not of clinical importance, whereas diastolic gallop rhythm is of great clinical significance. The author records the incidence of, and the influence of age, race and sex upon, diastolic gallop rhythm as deduced from a clinical and pathological study of 790 adult patients who died of heart disease. Of this series of patients 25·2% had had a gallop rhythm due to either auricular contraction or a third heart sound. Gallop rhythm occurred most frequently in hypertensive heart disease and coronary artery disease; indeed one in every three patients had this type of rhythm. *Cor pulmonale* was associated with gallop rhythm in about one case in five, and only one of ten patients who died of rheumatic heart disease or syphilitic heart disease had gallop rhythm. The average age at death of cardiac patients with gallop rhythm is less than the average age of cardiac patients without gallop rhythm. Coloured patients with fatal hypertensive heart disease and/or coronary heart disease, show a higher incidence of gallop rhythm than white patients. It is thought that this is really a manifestation of the influence of age, for the average age at death of the coloured patients was lower than that of the white patients. There was no demonstrable association between gallop rhythm and sex, but the association of this disorder with age was marked.

Renal Glycosuria.

H. BLOTNER AND R. W. HYDE (*The Journal of the American Medical Association*, June 12, 1943) found glycosuria at the time of military medical examination in 367 (or 0·8%) of 45,650 men aged from eighteen to forty-five years. Of these, 33 were shown to have renal glycosuria. There was a family history of diabetes in one-third of these, but only in 5·2% of a non-diabetic group. The occupations of most of the men were of a laborious nature. The authors express the opinion that persons found to have renal glycosuria should receive medical examination from time to time afterwards, because of the frequent incidence of diabetes in their families.

Significance of Systolic Cardiac Murmurs in College Students.

ANDREW W. CONTRATTO (*The New England Journal of Medicine*, April 22, 1943) examined 2,856 students at the Harvard University. A history of rheumatic fever was obtained in only thirteen cases. Five of the patients had no cardiac murmur, five had systolic murmurs which were barely audible and were confined solely to the pulmonary area; two had evidence of valvular heart disease, and one was classified as having possible mitral stenosis. A group of 26 students, previous to entering college, had been restricted in physical activity because of so-called "heart disease". Of these, seven had no murmur nor any other abnormal cardiac physical signs. Fourteen had only a very soft systolic murmur at the base or apex, without any other evidence of heart disease. Two had evidence of active rheumatic heart disease with valvular lesions and two had the physical findings of congenital heart disease. Thus 15% had organic heart disease. On the most careful examination 85% were found to have no heart disease. Thus it seems that a great many young persons are classified as having organic heart disease when it does not exist. Moreover, these young men are unnecessarily restricted from the usual activities of their age. In the entire group of 2,856 students a systolic murmur of some degree was heard in 350 cases (12·3%). In 7·3% of the total the murmurs were of such character and intensity that they were classified as functional by the examiner, and the subjects were therefore dismissed as having normal hearts. In 0·3% of the total, the cardiac findings led to a positive diagnosis of inactive rheumatic heart disease with valvular lesions; 0·2% had congenital lesions. The remaining 4·6% of the total had systolic murmurs of such intensity and location that they were not classified as suffering from functional conditions, nor were the findings sufficient to make a diagnosis of organic heart disease. The author concludes that the incidence of previous rheumatic fever and inactive rheumatic heart disease among Harvard College students is very low. Apparently, the diagnosis of organic heart disease is made too frequently when it does not exist. Likewise, the restrictions placed on persons with minor valve deformities is probably too rigid, and may inhibit an otherwise normal programme, both physical and mental.

Gall-Bladder Disease.

T. H. RUSSELL, R. F. CARTER AND E. OPPENHEIM (*The Bulletin of the New York Academy of Medicine*, February, 1943) discuss the ætiology, diagnosis and treatment of gall-bladder disease. Gall-bladder disease includes mainly organic lesions developed upon an underlying disturbance in structure and function. Gall-bladder disease is progressive; stones, infection, and obstruction of the gall-bladder, followed by common duct stones, infection, obstruction, cirrhosis of liver and spleen may occur in the course of time. Cholecystectomy usually cures the disease when it is limited to the gall-bladder, but it will not relieve the patient's symptoms when the sphincter of Oddi is the site of the difficulty. The spastic sphincter prevents the outflow of bile, and the tone of the gall-bladder increases to overcome this resistance. Gall-bladder diseases are divided into those with disturbed filling and emptying due to adhesions, pancreatic inflammation or tumour, and congenital abnormalities including abnormal cystic artery, and functional gall-bladder disease which is associated with increased resistance to the outflow of bile through the sphincter of Oddi (hypertonic dyssynergia) or diminished contractility of the gall-bladder. In the functional condition biliary pain and stasis occur, the pain being relieved at once by inhalation of amyl nitrite. The gall-bladder is enlarged and tubular; operation does not relieve the condition. When diminished contractility of the gall-bladder (hypotonic asynergia) occurs, the gall-bladder appears large and pear-shaped in radiographs with delayed emptying after a fatty meal. Other gall-bladder diseases are associated with disturbances in the concentrating function of the gall-bladder. Infectious cholecystitis is the most frequent. Reflux of pancreatic juice is an alleged cause of gall-bladder disease, and abnormal concentration of special elements, such as bile salts. Finally disorders in blood and metabolism give rise to gall-bladder disease, for example, hæmolytic icterus and cholesterol disorders of pregnancy and obesity.

A Microbe in the Blood in Glandular Fever.

R. A. WEBB (*The Lancet*, July 3, 1943) reports the isolation of *Listeria monocytogenes*, a microbe known to be capable of producing monocytosis in animals, by culture from the blood of a patient with glandular fever on the fourteenth day of the disease. He states that this is the third observation of its kind.

The Action of Potassium on the T Wave of the Electrocardiogram.

E. P. SHARPEY-SHAFER (*British Heart Journal*, April, 1943) has found that inversion of the *T* wave in the electrocardiogram due to myocardial infarction is increased when the serum potassium is increased, while flat or inverted *T* waves due to preponderance of a ventricle or myxœdema become upright. The author has found this fact useful in that it makes possible the analysis without delay of some electrocardiograms which are difficult to interpret without observation over a long period. He suggests that the inversion of the *T* wave in ventricular preponderance is more apparent than real and due to changes taking place in the *ST* interval and not in the mechanism that produces the *T* wave. The method employed to increase the serum potassium was to administer by mouth or stomach tube 15 to 20 grammes of a mixture of equal parts of potassium chloride and potassium citrate dissolved in about 250 millilitres of water.

Short Œsophagus with Peptic Ulceration.

P. R. ALLISON *et alii* (*The Journal of Thoracic Surgery*, June, 1943) describe ten cases of simple peptic ulcer of the lower end of the œsophagus. All the patients complained of dysphagia. The pain was felt behind the lower part of the sternum during deglutition: in some it seemed to rise up into the neck and in some it radiated through to the back between the shoulder blades. In each case the cause was found to be cicatricial stenosis of the œsophagus and simple ulceration. The ulceration was associated with chronic œsophagitis and gastritis. In each case

the narrowing of the œsophagus was associated with shortening, so that a part of the stomach was pulled up into the mediastinum. The authors make the suggestion that this deformity, usually referred to as congenitally short œsophagus, may be acquired and may be the result of ulceration and scarring. Dysphagia was dramatically relieved by œsophageal dilatation, but this had to be repeated from time to time.

The Treatment and Prevention of Thrombosis.

J. LEHMANN (*The Lancet*, May 15, 1943) has administered dicourmarin, which he also calls antiprothrombin or "AP", an anticoagulant first obtained from spoiled sweet-clover hay, by mouth to one hundred persons suffering from venous thrombosis in the lower limb and to 32 suffering from thrombophlebitis. In thrombosis the mean recovery time was reduced to one to three weeks, one-third of what it was before the drug was used, and in thrombophlebitis to six and a half days. The anticoagulant was also given prophylactically to 170 patients after various gynæcological operations; only one case of venous thrombosis and one case of mild embolism were seen; in a comparable series of patients the previous year fourteen had suffered these complications and three died. In about one patient among ten who received the anticoagulant hæmorrhages occurred, but in only 1 in 100 was it at all profuse, and in these it was readily controlled with vitamin *K* and blood transfusion.

Prophylaxis in Rheumatic Fever.

NORMAN H. BOYER (*The New England Journal of Medicine*, April 22, 1943) states that a specific agent for the prevention of rheumatic fever will probably not be available before the cause of the disease is known. Efforts must therefore be mainly directed towards the prevention of recurrences in patients known to be susceptible to rheumatic infection by virtue of previous attacks. The most widely held and best supported view of the pathogenesis of rheumatic fever at the present time is that certain persons, because of hereditary or environmental factors, or both, have developed abnormal tissue reactions to hæmolytic streptococci. The prevention of rheumatic attacks, therefore, is based largely on the prevention of hæmolytic streptococcus throat infections. Evidence has been gathered to show that susceptibility to rheumatic fever is transmitted as a single autosonal gene. According to the table compiled, if both parents have a positive history of rheumatic infection nearly all progeny will become afflicted. If one parent is positive and a grandparent on the other side of the family is positive, the expected incidence in the progeny is about 50%. If both parents are negative, but one grandparent of each line is positive, the expected incidence is about 25%. The author discusses the effect of climate on the incidence of rheumatic fever. He states that the bulk of evidence at present is certainly opposed to the routine removal of tonsils because of rheumatic susceptibility, even though Karser reported that the mortality rate was nearly twice as high in children whose tonsils were present at the time of the initial attack. There are no data indicating that large amounts of vitamin *C* or any other food substances have any specific beneficial action in the prophylaxis or treatment of rheumatic infection. Sulphonamides are ineffective in the treatment of the disease and patients are often made worse by the drug. Toxic reactions with high fever were commonly seen, and congestive heart failure was not infrequently precipitated. The use of sulphanilamide in the prophylaxis of rheumatic fever is an important advance in the control of rheumatic fever, and its administration is continued by some clinicians throughout the year for five years or longer after an attack of rheumatic fever. The use of salicylates and vaccines in prophylaxis is also discussed.

Death from Allergic Shock.

ERNEST L. HUNT (*The New England Journal of Medicine*, April 22, 1943) discusses a sudden death from an intradermal injection of a minute amount of guinea-pig hæmoglobin. The patient, a woman, aged twenty-two years, was given 0·2 cubic centimetre intradermally and died ten minutes later. She had had asthma for eight years. The family history was extremely important. The mother had asthmatic attacks and symptoms of hay fever during one summer. A brother was subject to hay fever and a sister to acne. A first cousin of the mother died in convulsions at the age of sixteen, ten minutes after a subcutaneous injection of diphtheria antitoxin; she also was an asthmatic and was the first person in the United States to die from an injection of diphtheria antitoxin. The author reviews the literature on the subject of death from allergic shock, and discusses the causation and the value of the Prausnitz-Küstner test as a post-mortem procedure. Persons hypersensitive to the proteins of small animals are put in the same category as those who are sensitive to horses, so far as the dangers of foreign-protein therapy are concerned. Use of the intradermal route for preliminary testing is discouraged.

Intolerance to Arsenical Drugs and Vitamin C.

K. D. LAHIRI (*Indian Medical Gazette*, March, 1943) shows that patients suffering from secondary syphilis excrete much less hippuric acid than normal subjects after a test dose of sodium benzoate. He also shows that they have a low vitamin *C* content in the blood. That intolerance of antisyphilitic arsenical drugs is related to the poor detoxifying capacity of the liver and the low vitamin *C* content of the blood is suggested by the following findings and by the response to treatment with vitamin *C*. Patients were divided into three groups according to their tolerance of arsenical treatment. The first group of twenty patients showed no intolerance, the second of twenty-four patients showed mild intolerance and the third group of eight patients showed severe jaundice or dermatitis from the arsenicals. The second group showed poorer results to the liver function test than the first group and the third group poorer than the second. The average vitamin *C* content of the blood for the three groups was: 0·473 milligramme of vitamin *C* per 100 cubic centimetres of blood for the first group, 0·304 milligramme for the second and 0·197 milligramme for the third group. The patients showing mild toxic symptoms were able to continue treatment without interruption if they were given 300 milligrammes of vitamin *C* intravenously before the arsenical injection. The syphilitic skin lesions of this group cleared up in from two and a half to four and a half weeks, while the lesions in the group who did not receive the additional vitamin *C* took from four and a half to seven weeks to clear up. The patients showing severe arsenical reactions were able to resume treatment with arsenic and vitamin *C* injections after twelve days of intensive treatment with liver extract and vitamin *C* given parenterally.

Libman-Sacks Disease.

EMANUEL LIBMAN (*The Journal of the Mount Sinai Hospital*, November-December, 1942) attempts to clarify the meaning of the Libman-Sacks disease—the various syndromes of which have caused confusion. The disease is a distinct nosological entity, the varying clinical pictures resulting from the involvement of different organs and systems. For example, cutaneous lesions such as *lupus erythematosus*, dermatomyositis, sclerodema, and/or petechiæ, may be associated with a characteristic endocarditis producing a systolic cardiac murmur. Pneumonitis, perivascular inflammatory foci, generalized adenopathy, glomerulonephritis, arthralgia, arthritis, fever, polyserositis, splenomegaly, anæmia *et cetera* may occur alone or in combination. Unity of the disease is established by the presence of the characteristic histo-pathological lesion—"hæmatoxylin-staining bodies", eosinophilic multinuclear coalescent bodies, endothelial bud capillaries, a signet cell lesion, as described first by Gross. The ætiology of the disease has not yet been established.

Besnier-Boeck-Schaumann Syndrome.

S. S. BERNSTEIN AND B. S. OPPENHEIMER (*The Journal of the Mount Sinai Hospital*, November-December, 1942) give a detailed study in analysis of the Besnier-Boeck-Schaumann syndrome, six cases forming the basis of discussion. The varying clinical picture is emphasized. In Case I diffuse adenopathy was present with failure of the right side of the heart due to diffuse pulmonary sarcoidosis, and skin lesions were present. In Case II the syndrome of uveo-parotitis was present with parotid swelling, generalized adenopathy, and impaired vision as a result of uveal tract involvement. In Cases III and IV there was adenopathy, especially of the hilar glands. In Case V, in addition to adenopathy, hepatosplenomegaly was present, whilst in Case VI adenopathy, irido-cyclitis and hepato-splenomegaly were found and the outcome was fatal. The unity and constitutional character of the syndrome were shown by the identical histopathological changes in all the cases. The characteristic absence of fever, the minimal constitutional symptoms, the duration of many months, the tendency towards spontaneous recovery, are emphasized. Radiotherapy was found of value in some of the cases.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on September 23, 1943, at Sydney Hospital. The meeting took the form of a number of clinical demonstrations by members of the honorary medical staff of the hospital.

Leontiasis Ossea.

DR. E. H. STOKES showed a man, aged thirty-two years, suffering from *leontiasis ossea*. The patient complained of frontal headaches of four years' duration; he said that when he was twelve years of age a swelling had appeared on the left side of the nose. Since that time the tumour had gradually increased in size, and during the past six months it had become painful to the touch. Recently his left nostril had become obstructed and his eyesight affected, apparently by the pressure of the bony masses. The patient was married and was the father of four children.

On examination, bosses were evident in both frontal regions, and a swelling was seen at the root of the nose on the left side. Appearances typical of *leontiasis ossea* were seen on X-ray examination. The blood serum reacted to the Wassermann test. Six intramuscular injections of "Rubyl", each of four cubic centimetres, had been given, and a slight diminution in the size of the swelling at the root of the nose had been observed. Dr. Stokes said that he had recently shown this patient at a meeting of the Section of Medicine, but he considered the condition of sufficient importance to warrant his showing the patient again, as it was rare and not usually accompanied by a positive reaction to the Wassermann test.

Diabetes Mellitus Complicated by Pulmonary Tuberculosis.

Dr. Stokes next showed a man, aged forty-one years, who had come to the hospital in January, 1942, because glycosuria had been noted at a medical examination for his admission to the military forces. The patient said that he had lost three stone in weight since January, 1941. He had noticed that he was passing excessively large amounts of urine and that his mouth was abnormally dry. He had suffered from a cough since December, 1941, and had expectorated blood on several occasions. He had been a heavy beer drinker, having consumed from six to twelve pints of beer per day.

The result of the glucose tolerance test was indicative of a severe type of *diabetes mellitus*. On January 16, 1942, an X-ray examination of the chest was made and the report was as follows: "Infiltration of the right upper lobe and some changes in the right lower lobe probably." Acid-fast bacilli were found in the sputum. The blood sedimentation rate was 42 millimetres in one hour. A dosage of thirty units of protamine zinc insulin per day was prescribed by Dr. Calov; but in spite of the improvement in the diabetic condition the pulmonary infection continued to advance, and on May 21, 1942, a report on an X-ray film was as follows: "Advanced tuberculous infiltration of the right lung with cavitation in the right upper lobe. Extension to the left lower lobe is also present." In June, 1942, however, the patient's condition began to improve, and the improvement had been progressive since that time. At the time of the meeting there was radiological evidence of fibrosis at the apex of the right lung, and the blood sedimentation rate was fifteen millimetres in one hour. Dr. Stokes remarked that he showed the patient because the association of *diabetes mellitus* and pulmonary tuberculosis was frequently of serious import.

Nail Dystrophy Treated with Vitamin B_1 Complex.

Dr. Stokes's third patient was a man, aged fifty-three years, who had been first examined on March 2, 1942. His chief complaint was that his finger nails were ridged and fissured in their long axes. He had lived for many years in north Queensland on a diet which was deficient generally in vitamins and particularly in vitamin *B*. The only abnormality noted on physical examination other than the condition of the finger nails, was an elevation of the arterial tension, the systolic blood pressure being 180 millimetres of mercury and the diastolic 100. The blood serum failed to react to the Wassermann test and Kahn's flocculation test produced a negative result. No arsenic was found in the patient's hair.

Vitamin B_1 was prescribed, in the form of "Vibex" tablets (Parke, Davis and Company) containing thiamin chloride, three milligrammes to be taken three times per day. Considerable improvement in the condition of the nails was noted after three months' treatment; but at the end of a further six months, as the condition was stationary, other constituents of the vitamin *B* complex, in the form of "Combex" capsules (Parke, Davis and Company) were prescribed. Two of these capsules were ordered three times per day. Immediate improvement was noted, and on May 3, 1943, the nails were normal. The number of capsules was reduced to three a day, and vertical ridges accompanied by fissuring recurred on two of the nails. Dr. Stokes said that it was proposed to increase the number of capsules again.

Clinical Photographs.

Dr. Stokes next showed a series of clinical photographs prepared by Mr. Appleby, the photographer to the hospital. They depicted the following conditions: a patient suffering from myxœdema and the same patient after six weeks' treatment; Hutchinson's teeth in a woman, aged thirty years; a patient with an eosinophilic adenoma of the pituitary body showing acromegalic features, and the X-ray film of the skull of the same patient showing enlargement of the *sella turcica*; koilonychia; a patient with a cerebello-pontine angle tumour, demonstrating involvement of the seventh nerve; a patient with obesity of the "pituitary" type, and the X-ray film of this patient's skull showing a very small *sella turcica*; and a man with ptosis resulting from *tabes dorsalis*.

Electrocardiograms.

Dr. Stokes's last exhibit consisted of two electrocardiograms demonstrating the importance of artefacts of extracardiac origin. The first showed the effect of muscular tremor of the left arm, and the second that of 50 cycle alternating current.

Huntington's Chorea.

DR. H. L. SPEARMAN, by courtesy of Dr. Evan Jones, Medical Superintendent of the Broughton Hall Psychiatric Clinic, showed a female patient, aged twenty-nine years, who had been clumsy in her movements for several years. She had always been "nervy", and had found it difficult to hold her positions. She was troublesome in the house, quarrelled with her sisters and father and took their things. She was irresponsible and had no idea of money value. She bathed and dressed herself frequently, sometimes she changed her clothes three times before lunch, and then went back to bed and to sleep. Changes in character had occurred, and she was irritable and eccentric. She was the eldest of a family of four. One sister had organic dementia with Parkinsonism, and was amiable and reliable. Her father was similarly affected with chorea.

On examination, the patient was seen to have choreic movements prominent in the face, neck and upper extremities. Excessive, loose, hypotonic, involuntary jerky movements occurred, and this motor unrest spread over the entire body. The speech was becoming explosive and the gait was ataxic. The tendon reflexes were brisk.

Huntington's Chorea Sine Chorea (Organic Dementia with Parkinsonism).

Dr. Spearman's second patient, also shown by courtesy of Dr. Evan Jones, was a female, aged twenty years, who complained that for three years she had noticed progressive lack of energy and grew so tired that she was unable to work or to walk far, or even to talk. She found her voice changed and had difficulty in pronouncing words. She was the second of a family of four. Her sister suffered from Huntington's chorea with moral defect, and her father suffered from chorea.

On examination, the patient was seen to have a dull, expressionless face with drooping eyelids. She was ataxic and walked on a wide base. Slowness of thought, word and action was present, and speech was monotonous and becoming indistinct. Mentally, poverty of ideas, retardation and depression were noted; no delusions were expressed, but sometimes the patient became suspicious. Slow nystagmus was present when she looked to the left; coarse tremor of the tongue, fine tremor of hands, increased tendon reflexes and Rombergism were also noted.

Dr. Spearman said that, according to Wilson, Huntington's chorea *sine* chorea had four characteristics: (i) chorea, (ii) dementia, (iii) a chronic, progressive course, (iv) onset in adult life (thirty to fifty years). Cases of chorea without dementia or of dementia without chorea had frequently been

reported. In the latter case the diagnosis was difficult in the absence of family history, the clinical picture being like that of *dementia paralytica* without the serological findings of that disease. The onset was not always in adult life; quite frequently it occurred in adolescence, and in such cases dementia appeared early, and usually the disease progressed rapidly to termination within a few years. It had been suggested that the chief determinants in Huntington's chorea behaved as Mendelian dominants, in which the motor and mental factors were separately inheritable and were more or less independent one of another.

The pathological background of the dementia was cortical degeneration (meningeal thickenings, generalized brain atrophy and loss of cells of the third layer of the cortex), most pronounced in the frontal lobes. The pathological conditions behind the motor manifestations pointed to striato-thalamic, strio-rubral and strio-cerebellar implication. Numerous autopsies had revealed changes in the lenticular region and losses in the putamen. Thus the motor symptoms had a pathological basis closely related to that seen in *paralysis agitans*. The chance of escape was about one in four at the best. In accordance with the law of dominants, a branch once free was always free.

Disseminated Sclerosis.

Dr. Spearman next showed a female patient, aged sixty years, who complained of failing vision, of difficulty in walking slowly or maintaining her balance on standing, of nervousness, and of inability to hold papers still in her hand, which shook and ached. The condition commenced in 1934 with severe pain in the left eye, and it had progressed gradually to the present state.

On examination, she was tremulous and ataxic. Rombergism was present. Atrophy of the temporal halves of optic disks, increased knee and ankle reflexes, and increased arm reflexes were noticed. The abdominal reflexes were absent, and vibration sense was absent at the tibial malleoli. The Wassermann test failed to produce a reaction.

Dr. Spearman said that the patient was shown to demonstrate the absence of Charcot's triad of nystagmus, intention tremor and scanning speech, and to illustrate the more modern triad of pallor of the temporal halves of the optic disks, absence of vibration sense at the tibial malleoli and absence of the abdominal reflexes. In addition, the onset late in life was noteworthy. Charcot's triad was usually present in Friedreich's disease, slight degrees of which, but with skeletal deformities, could be seen in the patient suffering from that disease whom he was about to show.

Friedreich's Ataxia.

The next patient shown by Dr. Spearman was a boy, aged fifteen years, who three years earlier had started to stumble and fall at times. His arms and legs shook when he was tired. A course of injections into the veins of the arm failed to relieve him. He could feed himself, but his fork jerked away wildly at times, and he had become bad-tempered. His brother, aged seventeen years, was affected in the same way, the trouble having commenced at the age of ten years; he was now in a wheeled chair and had to have his food cut up for him. His first cousin was similarly affected, and was in a wheeled chair at the age of sixteen years; the cousin was now aged twenty-eight years.

On examination, the patient was thin, and walked with an unsteady gait on a wide base. Slight nystagmus was present; the tongue made jerky movements, and speech was dysarthric. Dysmetria and slight intention tremor, general loss of muscle power, lordosis and *pes cavus* were present. Synergia, coordination and equilibration were grossly disordered. The knee and ankle reflexes were absent, the plantar reflexes were extensor in type, joint sensation was lost in the left hallux, and the vibration sense was impaired.

Dr. Spearman said that the condition had been diagnosed as juvenile *tabes dorsalis* and treated as such. No Argyll-Robertson pupil was present. Some form of Mendelian inheritance was usually present. In some cases permanent extension of the great toe was a feature.

Cervical Rib Pressure.

Dr. Spearman's next patient was a female, aged forty-one years, who complained of pain in the right shoulder and the neck of eight months' duration; the pain shot down the whole length of the arm to the fingers, but she did not remember which fingers were involved. The pain was most severe in the neck. Before the onset she was employed packing goods into boxes. In January, 1943, the type of work was changed to wrapping; the pain commenced a couple of weeks afterwards and was considered to be due to the change of work. It had continued much the same ever since, but the fingers were not now involved. The pain was worst at midday, and grew gradually easier when the patient was not working. She had no pain on Sundays. During the night she had to lie with the arm straight out to get relief.

On examination, slight wasting of the radial half of the thenar eminence was visible. It was not tender to pressure, but hyperæsthesia was present in the "anatomical snuff-box". Thermal sensation was normal. Loss of power was about 20% compared with the left hand; the patient was right-handed. The arm reflexes were brisk and equal. An X-ray film revealed slight enlargement of the transverse processes of the seventh cervical vertebræ.

Dr. Spearman said that three forms of accessory cervical rib were recognized: (i) enlarged seventh cervical transverse process; (ii) a short articulated rib with fibrous prolongation; (iii) a long, articulated, bony rib. The first two usually caused pressure symptoms. The enlarged process was commenest, and when it was associated with plexus pressure, it had a characteristic radiographic appearance, sloping down and out and tending to taper, the tip being the most sloping part.

Possible Muscular Dystrophy.

Dr. Spearman then showed a male patient, aged forty-seven years, who complained of loss of power in the legs and arms, commencing nine years earlier. At first he noticed weakness in his legs; one day he tripped and was unable to get onto his feet again without the aid of his hands. His walking distance gradually decreased. Three or four years later the weakness spread to the left arm and twelve months later to the right arm. The shoulders were first affected, and he found that he could not put his hands above his head, or button his braces behind him, and the braces caught on his shoulder blades. The right thumb and the forearms then became heavy and weak; he could not hold up the newspaper or manage his spoon. He could perform most things for himself and could even walk slowly and on level ground up to about four hundred yards. A brother was affected in the same way.

On examination, the patient was seen to be a small man showing great muscle wasting, most pronounced in the shoulder girdles, but also obvious in the face, hands and lower limbs. The scapulæ were "winged". A fine tremor of the face, chin, eyelids and hands was present. The arm and abdominal reflexes and the adductor reflexes were present; the knee and ankle reflexes were difficult to elicit, and the plantar reflex was flexor in type. The vibration sense was present.

Dr. Spearman said that the diagnosis in the case of the patient and his brother was not clear; both showed features of primary muscular dystrophy and of motor neurone disease.

Dr. Spearman, by courtesy of Dr. Dowe, of Strathfield, finally showed a male patient, aged fifty-four years, who had noticed a weakness in his legs eight years earlier; the legs used to swing like a pendulum. One year later the left arm became weak, and soon after the right arm was affected. Parkinsonism was diagnosed. In about six months most of his power appeared to return, and he had remained fairly well until two and a half years prior to the meeting, when he "collapsed" with severe pain in the right shoulder. In six hours he was unconscious. Disseminated sclerosis was diagnosed, and he spent seven months in bed. One year prior to the meeting he found that he was improving, and he believed that the improvement had been maintained, so that he was able to do five hours' linotyping per day. For shaving he used two hands; he brushed his hair with difficulty and was unable to put his right arm above his head. His braces fell and caught on his shoulder blades. If he lay down he could not get his breath, and he had to sleep propped up. The penis had withered and he was impotent. He believed that he was suffering from progressive muscular atrophy. A brother was affected in the same way.

On examination, the patient was seen to be a small man showing great wasting about the right shoulder girdle and the lower third of the left thigh. Lesser degrees of wasting were apparent in all his limbs and in the small hand muscles. The scapulæ were "winged". The arm reflexes were elicited with difficulty, and the leg reflexes were absent. Fibrillation was noticed in the buccinator and interossei muscles. The

abdominal reflexes were present, and the vibration sense was unimpaired. Dr. Spearman said that the diagnosis in the two cases discussed was not clear. In both features of muscular dystrophy and of motor neurone disease were present.

(To be continued.)

A MEETING of the Victorian Branch of the British Medical Association was held at the Royal Australasian College of Surgeons, Melbourne, on August 4, 1943, DR. J. A. CAHILL, the President, in the chair.

Upper Respiratory Tract Infection.

DR. F. M. BURNET read a paper entitled "Upper Respiratory Tract Infection" (see page 393).

DR. W. OSTERMEYER put in a plea for an alteration of the colloquial term "Urti"; he proposed "Urta" instead, in order to avoid the pronouncement that infection was inevitably present. The physiological reactions to temperature and humidity varied greatly in different subjects and caused symptoms, irrespective of the activities of germs or viruses.

DR. JOHN DALE described Dr. Burnet's address as an exposition of the subject which went as far as scientific knowledge permitted. He asked whether Dr. Burnet knew of any definite epidemics of influenza or common cold which had been proved to be bacteriological infections, and also whether methods of identification of common viruses had been applied in those epidemics.

Dr. Burnet said that there had been no such epidemics since the virus work had become practicable, and that in his view older reports needed overhauling in the light of present knowledge. The viruses of measles and of mumps were transmissible from monkeys with the production of recognizable similar lesions; but nothing was known of cough virus before 1933, and until some new knowledge of colds came to life there was no hope of progressing with that subject.

DR. D. O. ROSEBY commented briefly on the implications of Dr. Burnet's views, which were authoritative, and on the current methods of treatment, which were greatly at variance with the scientific facts.

DR. H. MCLORINAN asked Dr. Burnet if he could say why the Russians had chosen passive rather than active immunization.

Dr. Burnet replied that it had been shown by the Russians that a smaller amount of vaccine given intranasally produced successful protection; but he thought that their results were too good to be finally acceptable. Though it was claimed that one film of vaccine gave protection for three or four weeks, he himself could not explain why the protection should last more than three or four days. Naturally, there was no way of knowing when an epidemic of true influenza was coming.

DR. GUY SPRINGTHORPE asked whether the view was adopted that the virus of common cold lay dormant and became activated from time to time under meterological conditions which favoured activity.

Dr. Burnet said that no one knew where influenza went between epidemics. It might be of interest to recall that swine influenza virus lived in earthworms between times, and that the swine fed on the earthworm and that the influenza appeared in November. There might well be carriers of influenza and of common colds. In 1937, in Greenland, a shipload of isolated persons had no influenza for two months, and then a serious outbreak occurred, suggesting passage and increased virulence.

DR. HILDA BULL referred to Dr. North's experiments at the Commonwealth Serum Laboratories, from which it appeared that pertussis immunization was effective when the vaccine was sprayed into the nose. Dr. Bull asked whether there was a function of the nasal mucosa to produce antibodies better than they could be produced parenterally.

Dr. Burnet pointed out that he had been careful to make no claim that the intranasal application of vaccine was to be preferred to other methods.

DR. E. I. LITTLEJOHN asked how clinicians could differentiate between common colds and influenza.

Dr. Burnet replied that he was afraid the distinction was an epidemiological concept rather than a clinical one.

DR. JOHN SHAW asked whether there were any physical agents that acted as antiseptics against virus infection. He asked for an expression of opinion on the efficacy of ultra-violet irradiation.

Dr. Burnet cited propylin-guaiacol and ultra-violet rays as effective, but he doubted whether they were of practical value. He said that it was not worth using them everywhere, but it was a scientific fact that they would kill viruses.

Dr. Cahill, from the chair, drew attention to the address as evidence that the work at the Walter and Eliza Hall Institute of Research in Pathology and Medicine was up to world standards.

VICTORIAN BRANCH NEWS.

THE following letter is published at the request of the Medical Secretary of the Victorian Branch of the British Medical Association.

[COPY.]

THE INSTITUTION OF ENGINEERS, AUSTRALIA.

Melbourne Division.

Kelvin Hall,
55, Collins Place,
Melbourne, C.1,
2nd November, 1943.

The Secretary,
British Medical Association.

Dear Sir,

The attention of your association is directed to the second Conference on Political Affairs, the first of which was referred to in this division's recent invitation to you and your members to attend.

Special Conference on Political Affairs.

Second Conference: Friday 26th and Saturday 27th November, 1943.

This will be held in the Commerce Lecture Theatre, University of Melbourne, at 8 p.m. on Friday 26th and 3 p.m. and 7.30 p.m. on Saturday, 27th November.

As on the previous occasion, an evening meal may be obtained at Union House on Saturday by those who inform the Division Office (F 3323) not later than 23rd November. Ladies are invited to accompany members.

Friday Evening, 8 p.m.

Subject: China Today: The Dragon Awakes.

Speaker: Mr. N. D. Harper, M.A., B.Ed., Acting Senior Lecturer in History, University of Melbourne.

Mr. Harper is a student of Far Eastern affairs; he will illustrate his talk with a film strip showing modern developments in China; he is willing also to discuss the influence of China's awakening on the development of India.

For reference—Pringle and Rajchman—China Struggles for Unity (Penguin).

Saturday Afternoon, 3 p.m.

Subject: Russia: A New Civilization?

Speaker: Mr. I. F. G. Milner, B.A. (Oxon.), M.A. (N.Z.), Acting Senior Lecturer in Political Science, University of Melbourne.

The purpose of this talk will be to explain the system of government, and the economic and social planning underlying Soviet society, and to answer the question "Is Russia a Democracy?". Mr. Milner visited Russia in 1934 and can speak from personal impressions, as well as from an academic study of Soviet politics.

For reference—Bernard Pares—Russia (Penguin); Dean of Canterbury—Socialist Sixth of the World; Pat Sloan—Country with a Plan.

Saturday Evening, 7.30 p.m.

Subject: Politics and Economics in U.S.A.

Speaker: Dr. G. L. Wood, M.A., Litt.D., Acting Professor of Commerce, University of Melbourne. Dr. Wood, besides being a student of American affairs, visited the U.S.A. in 1934-1935 to study the New Deal at first hand.

Third Conference: Preliminary Announcement.

This will be held in the Commerce Lecture Theatre, University of Melbourne, on Friday evening and Saturday afternoon and evening, 10th and 11th December, 1943.

Yours faithfully,

(Signed) C. W. CANDY,
Honorary Secretary.

NOTICE.

THE first meeting of the Preventive Medicine Group of the Victorian Branch of the British Medical Association will be held at the Royal Australasian College of Surgeons, Spring Street, Melbourne, at 8.15 p.m. on Thursday, November 25, 1943. The speakers will be Professor R. D. Wright (Melbourne), Dr. F. W. A. Clements (Canberra) and Major Noel Gutteridge (Brisbane), who will discuss nutrition. All members of the British Medical Association are invited to attend.

Correspondence.

CONGENITAL DEFECTS IN INFANTS FOLLOWING INFECTIOUS DISEASES.

SIR: In the course of an investigation of congenital defects in infants following maternal rubella in pregnancy I have found, in a small series of cases, that lesions (hyalinization and sclerosis) are present in the glomeruli of the kidneys. In order to extend my researches, I would be very grateful if any of your readers possessing or later acquiring pathological material (eyes, kidneys *et cetera*) from such cases would send me specimens, together with a brief summary of the clinical history and findings. I would prefer tissues fixed in 10% formol-saline.

My colleague, Dr. Tostevin, has noted that the teeth of some of these children appear to be abnormal. Specimens of teeth, either erupted or unerupted, would also be acceptable.

Yours, etc.,

CHARLES SWAN.

Institute of Medical and Veterinary Science,
Adelaide,
October 27, 1943.

EXTRACTION OF CATARACT IN ITS CAPSULE (TOTAL EXTRACTION).

SIR: Dr. R. A. de Castro Basto is to be congratulated on his brilliant results when following the Stanculeanu-Knapp-Torok-Elschnig technique for the intracapsular extraction of the cataractous lens (THE MEDICAL JOURNAL OF AUSTRALIA, October 16, 1943).

The English school of ophthalmic surgery is well known for its conservatism, and it is not at all surprising that oculists in this remote outpost of Empire should still cling tenaciously to methods long since discarded by their more astute continental colleagues.

From Dr. Basto's figures it would appear that eighteen of his forty patients, that is, 45%, regained a visual acuity of $^6/_{12}$ or less. An acuity of $^6/_{12}$ in the aphakic eye is not comparable to $^6/_{12}$ in the normal because of the alteration in size of the retinal image. If the patient does not regain more vision than this he is not able to read in comfort, and usually expresses disappointment at the result. For this relatively poor result we cannot blame the Stanculeanu-Knapp-Torok-Elschnig technique as there are no capsular remnants left to block the pupil. The fault must lie in the fundus. Here one must confess that it is the experience of many surgeons who still use the much more crude technique of extracapsular extraction, that 50% of their patients can read with a fair amount of comfort. My own experience has been that needling is not required nearly as often as Dr. Basto would suggest. I have always been prone to assume that if a clear, undistorted view of the fundus is obtainable after an extracapsular extraction, a needling will not improve the visual acuity. With cases which after ten years of needling still have satisfactory vision, it is quite obvious, in view of Dr. Basto's remarks, that some lucky chance must have favoured the surgeon.

I have seen an oculist on occasion, a little more daring than usual, remove an immature cataract, and even a complicated one by the "classical" method. Strange to say, the results were quite good, although such flying in the face of providence, if persisted in, can have only one outcome.

It requires a little more courage than most of us posseses to operate on both eyes at once. Again, if a successful result were to follow a cataract extraction on one eye, many would hesitate to operate at a later date on the other eye if the warning were given by the presence of defective light projection that a failure would result. Under certain circumstances the pocket of the surgeon might become a little heavier, and, as a well-known writer has said of outstanding historical events, the operation would thus prove to have been "a good thing".

Yours, etc.,

KEVIN O'DAY.

33, Collins Street,
Melbourne,
October 29, 1943.

ANTENATAL SUPERVISION.

SIR: It is to be hoped that your leading article, "Antenatal Supervision", in THE MEDICAL JOURNAL OF AUSTRALIA, October 30, 1943, will receive the careful attention of all engaged in the practice of obstetrics and those occupied in the teaching of medical students and obstetric nurses that it so thoroughly deserves.

F. J. Brown in his latest book on antenatal and postnatal care states: "It is the fashion today to decry antenatal care and to charge it with having failed in its purpose . . . if antenatal care has failed it is not because it is inherently useless, but because it has comparatively seldom been given a chance by being properly practised."

In my opinion it is in the toxæmias we have most noticeably failed, and failed because we have neglected those points you have so clearly defined, notably prompt action immediately on the first appearance of the faintest cloud of albumin and not waiting till the patient is severely ill.

Yours, etc.,

H. A. RIDLER.

Sydney,
November 1, 1943.

THE MEETING OF THE FEDERAL COUNCIL.

SIR: Dr. Hunter accuses me of not acquainting myself with the matters and evidence which were before the Federal Council of the British Medical Association and holds me to blame for this. In the immediately preceding sentence he states that the report of the meeting published in your columns was incomplete; it is very difficult to see, therefore, how a member of the profession can obtain the facts about the meeting of the Council if the report of the meeting omits important and relevant material. The origin of the report may be guessed from Dr. Hunter's antepenultimate paragraph where he states in one sentence that the report by the New South Wales Branch of the Association on rehabilitation did not reflect on present methods of treatment, and states in the final sentence that the adoption of the methods recommended would benefit the community. Not having the factual and statistical information on which Dr. Hunter bases this conclusion, I did not state, as Dr. Hunter suggests, that the report reflected on the efficacy of present methods of treatment. Surely if present methods can be improved, that is a reflection on them.

Dr. Hunter bitterly attacks me for recording impressions from an impressionistic report, but in his last paragraph retains the right for others to be influenced by impressions. He assures us that the Council also had factual and statistical information before it: the only sample included in the report did not inspire confidence.

We would do well to remember that THE MEDICAL JOURNAL OF AUSTRALIA finds its way into many overseas libraries. In a recent number of this journal I have had occasion to comment on inaccurate reporting of Australian material to overseas journals. It is just as important that Australian material reported in THE MEDICAL JOURNAL OF AUSTRALIA should be concise, accurate and as factual as possible. If my letter stimulates people to attain this objective, then it will have done a service to the profession.

It is well to recall also that in these days people other than the profession obtain and read reports such as the one in question. Our reporting should be such that these people will not laugh when the profession claims a high level of clear thinking.

Yours, etc.,

R. DOUGLAS WRIGHT,
Professor of Physiology.

University of Melbourne,
November 3, 1943.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 234, of November 4, 1943.

CITIZEN NAVAL FORCES OF THE COMMONWEALTH.

Royal Australian Naval Reserve.

Appointment.—Peter Ronald Brett is appointed Surgeon Lieutenant, dated 5th October, 1943.

ROYAL AUSTRALIAN AIR FORCE.

Citizen Air Force: Medical Branch.

Flight Lieutenant A. G. Gibson (256822) is transferred from the Medical Branch Reserve to the Active List for part-time duty with effect from 13th September, 1943.

Flight Lieutenant A. J. Harker (261287) is granted the acting rank of Squadron Leader whilst occupying a Squadron Leader post with effect from 9th July, 1943.—(Ex. Min. No. 299—Approved 27th October, 1943.)

Reserve: Medical Branch.

Flight Lieutenant J. B. Cahill (263188) is transferred from the Active List with effect from 30th September, 1943.—(Ex. Min. No. 296—Approved 27th October, 1943.)

The following are appointed to commissions on probation with the rank of Flight Lieutenant with effect from 13th September, 1943: Charles Reginald Dines, M.B., B.S. (277458), Bryan Thomas Dowd, M.B., B.S. (267562).—Ex. Min. No. 298—Approved 27th October, 1943.)

CASUALTIES.

ACCORDING to the casualty list received on November 2, 1943, Captain T. Le Gay Brereton, A.A.M.C., Turramurra, New South Wales, who was previously reported to be missing, is now reported to be a prisoner of war.

THE "PERFECT" TEAPOT.

EARLY in 1929 some thousands of doctors throughout Australia procured what was known as the "perfect" teapot. It was described in this journal in the issue of March 16, 1929. Special arrangements were made regarding its distribution among medical practitioners. After the lapse of time it is only reasonable to expect that the teapots may now need reconditioning in order to get the best results from the brewing of tea. We are advised by the Challenge Silverware Department of Robur Tea Company, Limited, Clarendon Street, South Melbourne, that although not permitted under wartime conditions to manufacture new plated-ware, they can repolish and replate existing teapots so as to make them as good as new to give years of further service. Inquiries addressed to the company will receive prompt attention.

Obituary.

COSMO WILLIAM FOWLER.

WE regret to announce the death of Dr. Cosmo William Fowler, which occurred on November 6, 1943, at Waverley, New South Wales.

Medical Appointments.

Dr. Doris Lyne Officer has been appointed a member of the Queen's Memorial Infectious Diseases Hospital Board.

Books Received.

"Whooping Cough", by Joseph H. Lapin, B.Chem., M.D.; 1943. Springfield: Charles C. Thomas. London: Baillière, Tindall and Cox. 9" x 5¾", pp. 249, with 64 illustrations. Price: $4.50.

Diary for the Month.

Nov. 16.—New South Wales Branch, B.M.A.: Ethics Committee.
Nov. 17.—Western Australian Branch, B.M.A.: Branch.
Nov. 18.—New South Wales Branch, B.M.A.: Clinical Meeting.
Nov. 23.—New South Wales Branch, B.M.A.: Medical Politics Committee.
Nov. 24.—Victorian Branch, B.M.A.: Council.
Nov. 25.—New South Wales Branch, B.M.A.: Branch.
Nov. 26.—Queensland Branch, B.M.A.: Council.
Dec. 1.—Victorian Branch, B.M.A.: Branch.
Dec. 1.—Victorian Branch, B.M.A.: Council.
Dec. 1.—Western Australian Branch, B.M.A.: Council.
Dec. 2.—New South Wales Branch, B.M.A.: Special Groups Committee.
Dec. 2.—South Australian Branch, B.M.A.: Council.
Dec. 7.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
Dec. 7.—New South Wales Branch, B.M.A.: Organization and Science Committee.
Dec. 8.—Victorian Branch, B.M.A.: Council.
Dec. 9.—New South Wales Branch, B.M.A.: Branch.
Dec. 10.—Queensland Branch, B.M.A.: Annual Meeting.
Dec. 14.—New South Wales Branch, B.M.A.: Ethics Committee.
Dec. 14.—Tasmanian Branch, B.M.A.: Branch.
Dec. 17.—Queensland Branch, B.M.A.: Council.
Dec. 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility unless such a notification is received within one month.

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Inquiries from and applications to the undersigned.

Applications close 22nd November, 1943, at Perth.

GEO. W. SIMPSON,
Public Service Commissioner.

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(Sgd.) GEO. GOUGH,
Secretary and Business Manager.

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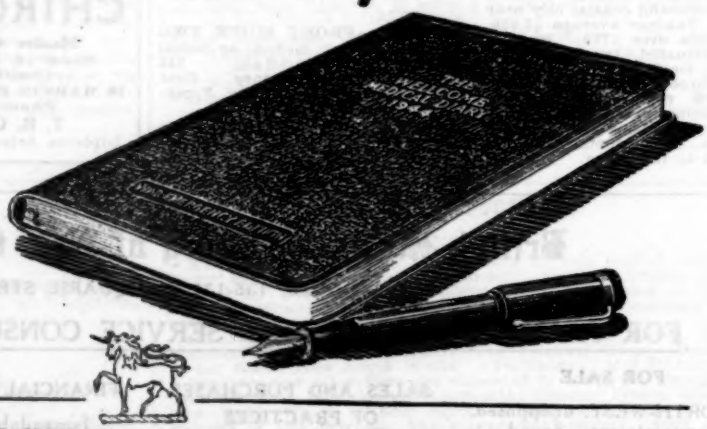

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